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SCREENING PROSTATE SPECIFIC ANTIGEN EFFECTS ON RACIAL DISPARATE MORTALITY: A PROPENSITY SCORE ANALYSIS

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A proposal submitted in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy at Virginia Commonwealth University

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"Never regard your study as a duty, but as the enviable opportunity to learn the liberating beauty of the intellect for your own personal joy and for the profit of the community to which your later work will belong". A statement given to the Princeton University freshman publication, *The Dink*, 1933, Albert Einstein.

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ABSTRACT

SCREENING PROSTATE SPECIFIC ANTIGEN EFFECTS ON RACIAL DISPARATE MORTALITY: A PROPENSITY SCORE ANALYSIS

By R. David McNally, Ph.D., M.S.H.A.

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University.

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Prostate cancer is the most commonly diagnosed cancer among men in the United States. It is frequently cited that racial disparities in mortality between Caucasian and African American men with localized prostate cancer exist. In addition, the question of whether prostate cancer screening with the prostate specific antigen blood test (PSA) leads to reduced mortality remains unanswered. Outcomes theory and survival analysis have shown controversial inconsistencies in support of early detection methods for prostate cancer to the extent that experts in the medical community do not agree on best-practice guidelines suggestive of eliminating such disparities and reducing mortality.

The purpose of this study was to explore the relationship between screening PSA tests and racial differences in mortality among Caucasian and African American men

with application of a propensity scoring analysis on a large population-based data set. Prostate cancer patients diagnosed from January 1, 1986 through December 31, 2006 (n = 515,802 cases) from the SEER-17 data set linked to Medicare claims files were included. A separate analysis using a 5% randomized group of over 263,000 men without prostate cancer was also examined.

The results demonstrated that no statistically significant differences in mortality between Caucasians and African Americans in the prostate cancer group existed ($p=0.993$). Further, the same result was found among men from the 5% randomized group without prostate cancer ($p= 0.832$), that no statistically significant difference exists for this study population when using a propensity scoring analysis and a conditional Cox regression model. From both analyses, no survival benefit was found for screened men versus non-screened men when using the PSA test for early detection. In addition, because age is a well-known predictor of death, a separate analysis was performed on age-matched men. The results for the age analysis also demonstrated no statistically significant differences in racial mortality or whether screening PSA reduced mortality after applying a propensity scoring analysis to a conditional Cox regression model.

In conclusion, it is believed that using a propensity scoring method and Cox regression analysis improved the evaluation of this large population data set where censoring for survival time was important and where matched pairs were utilized. Further work in health services research using large population-based data sets should be pursued and incorporating Cox regression with a propensity analysis can be helpful.

CHAPTER 1: INTRODUCTION

Overview of Prostate Cancer

The American Cancer Society (ACS) estimates that 217,730 new cases of prostate cancer in men of all races would be diagnosed in 2010 making prostate cancer the most commonly diagnosed cancer among men in the United States. The ACS reported in 2010 that almost 63% of all prostate cases are diagnosed in men over 65 (ACS, 2010). However, the 2010 estimate is 13% higher than 2009 (217,730/192,280) yet still remains approximately 1% lower for new cases that were expected in 2007 (218,890). A reason for the decrease from 2010 and 2007 may reflect changes in prostate screening habits and improved treatment strategies in surgery and radiation therapy over the past few years. For example, cancer screening educational initiatives aimed at increasing men's knowledge about possible benefits from early detection and aggressive treatment have increased throughout communities. Improved imaging techniques and new technologies in surgery such as robotic prostatectomy for improved nerve sparing and brachytherapy and intensity modulated radiation therapy treatments in radiation therapy are being implemented to provide greater access to new and aggressive treatment (ACS, 2010; ACS, 2009). The estimated number of deaths from prostate cancer in men of all races for 2010 (32,050) represents 11% of all cancer deaths, second to lung and bronchus cancers which account for 29% of cancer deaths (ACS, 2010). Although previous estimates

illustrated decreases in both the numbers of new cases and deaths, the number of estimated new prostate cases in 2010 increased by 13% over 2009 with the estimated percentage of deaths from prostate cancer for the same period also rising by 17% for all races (32,050/27,360) (ACS, 2010). The estimated cases found in the **ACS Facts and Figures** report for 2010 are based on 1995-2005 incidence rates from 41 states and the District of Columbia as reported by the North American Association of Central Cancer Registries (NAACCR) for men of all races and does not include a separate statistical result for Caucasians. The estimated numbers of deaths are based on data from the U.S. Mortality Public Use Data from 1969-2006 reported by the National Center for Health Statistics, Centers for Disease Control and Prevention, 2009 and also does not include separate statistics for the Caucasian race. The report does include separate statistics for other races, such as African American: Table 1 shows a similar trend expected for African American men with estimated deaths from prostate cancer for 2009/2010 projected at 3,690 or 13% fewer than the estimated death rate for the 2007/2008 period at 4,240. However like new cases and deaths for all races, estimates indicate that African Americans will experience a significant increase in the number of new cases and cancer deaths for the 2011-2012 period (see Table 1) (American Cancer Society-African Americans [ACS-AA], 2007-2008, 2009-2010, 2011-2012).

Although death rates have fallen more quickly for African American men than for Caucasian men since early 1990, the death rate for African American men remains more than twice that of Caucasian men. These varying rates may be due in part to differences

Table 1. Estimated Total of New Prostate Cancer Cases and Deaths 2008-2010 (all races) and African American Cases 2008-2012.

Year	Total new cases	% new cases (yearly)	Total deaths	% deaths (yearly)	African American new cases	% new cases (yearly)	African American deaths	% deaths (yearly)
2008	186,320		28,660		30,780		4,240	
2009-2010	192,280	3.2%	27,360	-4.5%	27,130	-12%	3,690	-13%
2011-2012	217,730	13.2%	32,050	17%	35,110	29%	5,300	44%

Source: American Cancer Society, 2010; American Cancer Society – African American Men, 2009-2010, 2011/2012.

in treatment choices, screening habits, and education about prostate cancer among the races (ACS-AA, 2011/2012; National Centers for Health Statistics, 2006). The disparity also translates into poorer survival rates in African American men who tend to present with advanced stage disease and have less access to appropriate and timely treatment. For example, Figure 1 shows death rates for both African Americans (dark line) and Caucasians (light line) increasing from 1975 through 1988 where for African Americans the rate increased more sharply to nearly 70 per 100,000 and only slowly rising to 33 per 100,000 for Caucasians. After 1988, the rates began to rise again for both races; however, the increase was much greater for African Americans. For instance, Figure 1 shows the

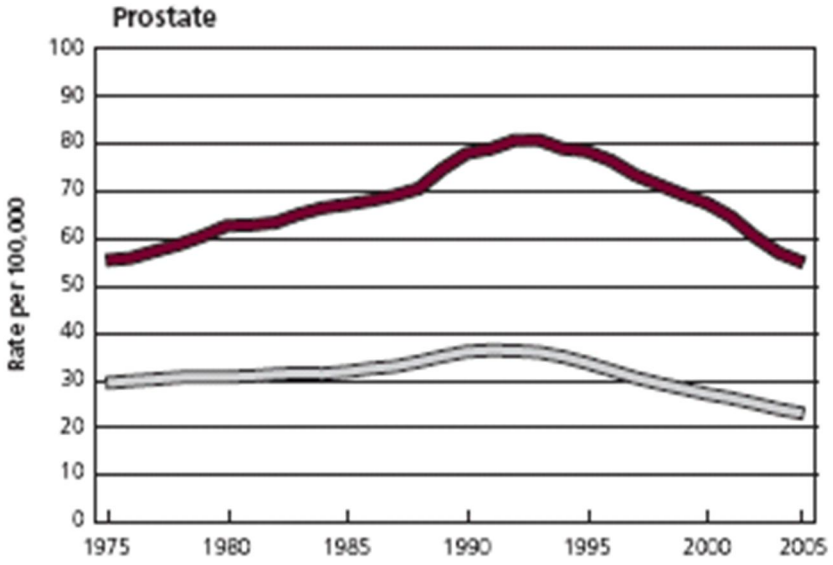

Figure 1. Trends in death rates for African American (dark line) and Caucasian men (light line) with prostate cancer, 1975-2005. source: National Center for Health statistics, Centers for Disease Control and Prevention, 2008.

rates peaked near 81 per 100,000 African Americans and 38 per 100,000 Caucasians around 1993 at which time they began to fall.

The rates for African Americans decreased much faster than for Caucasians through 2003; however, they still remained more than 2.4 times greater as demonstrated in Figure 1. Finally, by 2005 the death rates for African Americans and Caucasians fell to near 55 and 22 per 100,000 men, respectively. Similar rates were reported by the National Cancer Institute's Surveillance, Epidemiology, and End Results data (SEER). These rate changes may reflect increased prostate specific antigen (PSA) test utilization during the same period, as the dissemination of the test grew quickly throughout the U.S. after its first introduction in 1986 as a screening tool.

The National Cancer Institute's (SEER) Cancer Statistics Review provides information on incidence, mortality, and prevalence of disease in the United States. In a review of prostate cancer trends using the SEER-Medicare data from 1973-1995 it was reported that the burden of prostate cancer is carried mostly among elderly men and African American men. The median age in men diagnosed with prostate cancer was 71 and the median age at death was 78. In addition, more than 75% of all cases of prostate cancer were diagnosed in men over 65 with greater than 90% of deaths occurring in this age group (Harris & Lohr, 2002). In a more recent review from 2000-2004, the SEER-Medicare data suggests that the median age at diagnosis for prostate cancer during that period was 68 with the median age of death reported to be 80 (National Cancer Institute [NCI], 2008). Differences in age at diagnosis between the two datasets are explained by the increased use of screening to detect earlier stage disease in younger men (ACS, 2008; ACS, 2009; Harris & Lohr, 2002).

The SEER report also compared cancer incidence rates and death rates between African American and Caucasian men. The report noted an incidence rate of 258.3 to 163.4 (1.6 rate ratio) and a death rate of 64 to 26.2 (2.4 rate ratio) for African American to Caucasian men per 100,000, respectively. Therefore, African American men are 1.6 times more likely to develop prostate cancer and 2.4 times more likely to die from prostate cancer than Caucasian men.

A review sponsored by the U.S. Environmental Protection Agency (EPA) in 2004 also expressed concerns over increased incidence rates of prostate cancer by noting significant differences among African American men and Caucasian men. In addition, the

ACS-AA noted similar significant incidence rate differences from 1975 through 2005 for African American and Caucasian men, suggesting that a racial disparity may reflect higher incidence rates for African American men than for Caucasian men. Both reports claimed that increased incidence could be related to early detection by screening thus resulting in increased numbers of cases including those of more aggressive disease as well as more indolent prostate cancers.

Definitions and Terminology

Prostate Gland

The prostate gland is part of the male reproductive system and surrounds the urethra, a tube that empties urine from the bladder and carries semen during ejaculation. The prostate's main purpose is to produce fluid for semen in order to transport sperm. Normally, it is the shape of a walnut or crab apple and weighs only a few grams. It is located in front of the rectum, behind the pubic symphysis, beneath the bladder and is divided into three parts or zones (see Figure 2). The tissue immediately surrounding the urethra and down the center is the transition zone. The transition zone is the area of prostate tissue that grows during a non-cancerous condition known as benign prostatic hyperplasia (BPH).

Benign prostatic hyperplasia is the most common non-cancerous growth process in men (Carter, 2007). It is more commonly found in western countries (i.e., United States, United Kingdom, and Canada) rather than eastern countries (i.e., Japan and China). Within the U.S., BPH is more commonly seen in African American men

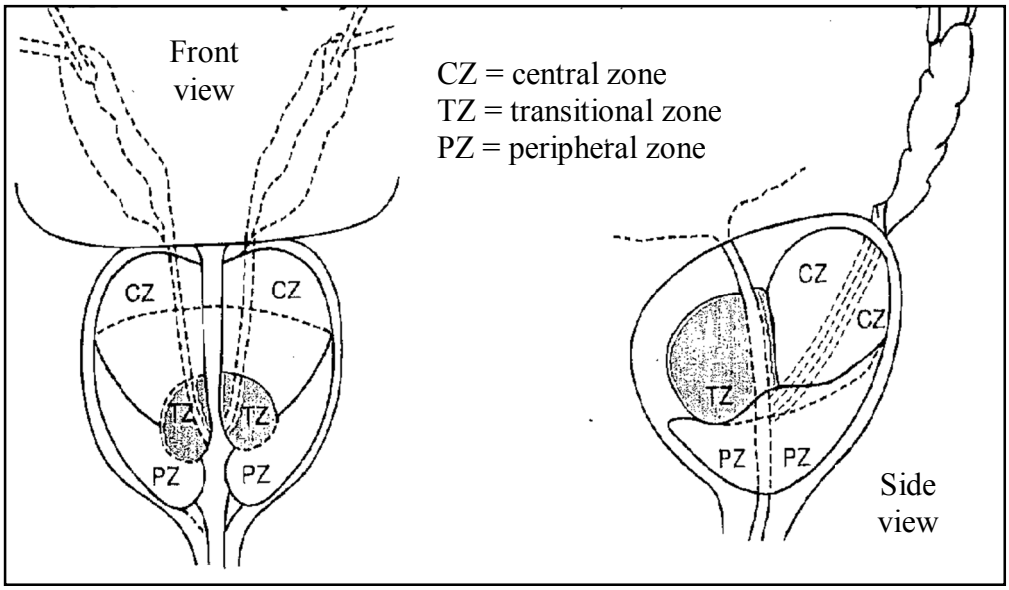

Figure 2. Illustration of prostate zones. CZ central, TZ transitional, and PZ peripheral zone.

than in Caucasian men (Carter, 2007). The central zone lies outside the transition zone and the largest and outermost zone is called the peripheral zone. It is the peripheral zone in which most cancers are found. The prostate gland is encapsulated within a fibrous tissue (Carter, 2007; ACS, 2008; ACS, 2009; ACS-AA, 2007/2008) (see Figure 2).

Screening Tests

Population or mass screening programs are meant to detect early stage cancers with the goal of curing disease (reducing mortality) and improving outcomes (quality of life issues). These programs are designed to examine asymptomatic men at risk. In contrast, early detection or opportunistic screening is guided toward the patient and his physician usually initiated by one or the other at the time of consultation and from resulting symptoms experienced by the patient. Opportunistic screening is a setting where

patients have not been invited to participate in a study protocol or are not part of an organized population-based screening program (Schmidt, Riesen, & Prikler, 2004; Legler, Feuer, Potosky, Merrill & Kramer, 1998).

Generally, men with localized prostate cancer have no symptoms; however, slowing of urinary flow, having to void during the night (nocturia), and increased urinary frequency can be common low grade symptoms. These are some of the same symptoms experienced by aging men without prostate cancer. It is for these reasons that early detection tests were developed in order to identify prostate cancer while it remains confined to the gland itself. However, to date, there remains controversy with the idea of early detection by screening. The three most commonly used tests are a blood serum prostate specific antigen (PSA), a digital rectal exam (DRE), and transrectal ultrasound imaging (TRUS) (ACS, 2008; ACS, 2009; ACS-AA, 2007/2008; Challen, 1998). It is suggested that use of any of these tests on their own may result in low sensitivity, specificity, and decreased positive predictive value for prostate cancer detection and that more favorable results could be obtained by using a combination of the three (ACS, 2009; ACS-AA, 2007/2008, American Urological Association [AUA], 2009, Carter, 2008).

Prostate Specific Antigen

Prostate specific antigen is a protein produced within the prostate gland that is easily measured when found in the bloodstream. Every man has some concentration of PSA in the bloodstream that varies with many factors, including age. Other factors associated with increased serum PSA values could include a recent DRE where palpation

of the gland itself may cause a rise in PSA. More factors include biopsy, transurethral resection, urinary retention, prostatitis, and ejaculation. Physical exercise has not been associated with increased PSA levels (Schmid et. al, 2004; Challen, 1998). Increased PSA levels can indicate prostate problems and even cancer; however, elevated levels are not always indicative of prostate cancer.

The PSA test was first approved by the Food and Drug Administration (FDA) in 1986 as a method to determine the success of treatment in men who have cancer and to monitor the gland for cancer recurrence and not initially as a screening tool. Currently, the PSA test is used in the United States as a means of early detection and has been credited by advocates of screening as the reason why prostate cancer incidence and mortality rates are declining (ACS, 2008; AUA, 2009; American Medical Association [AMA], 2007). However, it remains unclear whether the test reduces prostate cancer-specific death rates. In fact, some have criticized use of the test because most men with an elevated PSA do not have cancer. These ideas are continually debated and remain controversial (Carter, 2007; ACS, 2009, ACS-AA, 2007/2008). The major disadvantage of the PSA test is its lack of specificity and sensitivity, where sensitivity for screening tests is defined as the ability of a test to detect cancer that would have been diagnosed in the future in the absence of the screening test. It is has been noted that 25% of prostate cancer patients show no elevated PSA level and that in order to define the true value for both the sensitivity and specificity of the test, that all prostate glands would have to be removed and evaluated pathologically (Schmid, 2004; Hakama, Auviven, Day & Miller, 2007). In a separate report using SEER-Medicare data, the authors noted that 18-39% of

white men and 20-44% of African American men were over diagnosed by use of the PSA test (Schmid, 2004), and one study of veterans concluded that PSA screening rates among elderly men were higher than men of other age groups (Walter, Bertenthal, Lindquist & Konety, 2006). The term over diagnosed suggests that screening may detect cancers that would have never been diagnosed in the absence of screening and which could potentially lead to unnecessary treatment (Draisma, Boer, Otto, Van der Cruijsen, Damhuis & Schroder, 2003). A more formal definition of the term over diagnosis includes detecting indolent non-aggressive cancers that would have never become clinically evident without screening (Ciatto, Gervasi, Bonardi, Frullini, Zendron, Lombardi et. al, 2003).

Digital Rectal Exam

A digital rectal examination (DRE) is an examination by a physician who places their index finger inside the rectum to feel the surface of the prostate gland. The gland sits anterior to (in front of) the rectum thus making palpation easy with only minor discomfort. The physician notes any hard nodules (surfaces) or irregularities in shape that may indicate prostate cancer based on volume and gland size.

Volume measurements can be verified manually during the DRE. Specifically, measurements are determined once physicians have first, noted landmarks and have identified abnormalities by palpating the gland, they would then move the index finger across the furrow to the right and left lateral sulcus adding the numbers of finger widths it took to cross the full width of the gland. This dimension provides the width in centimeters (cm) as most fingers tend to be close to one centimeter across. The physician

would then move the finger over the surface of the gland in the length direction from the apex to the base while estimating the numbers of fingernails. This method is used to estimate the length because most fingernails also tend to be approximately one centimeter across (Zackrisson, Aus et al., 2003; Pinsky et al., 2006). If the DRE is used alone, it can miss 30-40% of prostate cancers (Carter, 2007; ACS, 2009, ACS-AA, 2007/2008). If abnormalities are noted, further testing is indicated usually through an ultrasound study to define the prostate volume and biopsy for pathological confirmation.

Transrectal Ultrasound and Prostate Biopsy

Typically, should a patient have an elevated PSA and/or abnormal DRE, the physician would order further pathological work up in the form of a transrectal ultrasound and then a tissue biopsy in order to confirm presence of disease. During transrectal ultrasound imaging the prostate volume can be measured and any irregularities visualized. For biopsies, the method of obtaining the tissue is typically through the use of a biopsy needle under the guidance of ultrasound imaging. The physician positions the biopsy needle affixed to the probe using ultrasound imaging, guides the probe to specifically identified regions within the gland, and punctures the gland by triggering the needle. This method removes a small tissue core that is placed into a container for later evaluation and observation of tumor characteristics by a pathologist to determine if cancer is present (Carter, 2007; ACS, 2009, ACS-AA, 2007/2008).

Tumor Characteristics

Grade

Tumor aggressiveness is determined by examining the microscopic pattern of cells obtained from biopsy tissue samples. The most common type of tissue biopsy is called a sextant biopsy where a physician obtains tissue samples from six different regions within the prostate gland: three samples from the right lobe and three from the left lobe. When cancer is confirmed by biopsy, a pathologist grades the disease based on specific cell characteristics. The most common grading system is known as the Gleason scoring method. The Gleason score method assigns a numerical value to each of the six tissue core samples and can range from 1 (least aggressive) to 5 (most aggressive) based on extent of tumor cell differentiation within a core sample (Gleason, 1977). Typically, the Gleason score is displayed as the sum of two numbers from the two most common patterns of tumor visualized by pathology. For example, 3 + 4 = 7 would indicate a Gleason score 7, from summing the most common tumor pattern seen in a single core sample and the second most common tumor pattern within a separate core sample. Given that the Gleason score can range from 1 to 5, the added values can range from 1+1 to 5+5 or from 2 to 10. The majority of detected tumors range from 5 to 10. The Gleason score is believed to be the most important predictor of disease extent and overall prognostic outcome (ACS, 2009; AUA, 2009; Carter, 2007).

Stage

Tumor stage is the extent to which the tumor has involved the prostate gland or spread outside the gland. The American Joint Committee on Cancer (AJCC) has

established a system of tumor staging. For instance in localized/regional disease, stage 1 indicates tumors of T1, T1a, T1b, and T1c grade and with no known nodal involvement (N0) and no known metastasis or spread of disease (M0). According to AJCC nomenclature, this study will focus only on clinical Stage 1 and Stage 2 tumors of T1 or T2, N0, and M0 since 88% and 92% of prostate cancers diagnosed in African American and Caucasian men respectively are staged with localized/regional disease (ACS-AA, 2007/2008).

Risk Factors

Consensus for risk factors associated with prostate cancer varies; however, the ACS identifies age, ethnicity, family history, and socioeconomic status as the greatest factors to which aggressive disease can be attributed. African American and Jamaican men of African descent have the highest incidence rates worldwide (ACS, 2010). Family history has consistently shown to be a significant risk factor with positive association of two to three times more likely for men to develop prostate cancer when they have first degree relatives with prostate cancer, such as a father, brother, or son. However, some studies suggest that this association may be contaminated by selection bias claiming that clinical and pathological features of familial cancers are similar to nonfamilial cancers (Bostwick et al., 2004; U.S. Preventive Services Task Force, [USPSTF], 2002; Whittemore, 1995).

Socioeconomic factors may also influence prevention and early detection methods, treatment choices, quality of life, and survival. Approximately 24% of African Americans live below the poverty level compared to only 10% of Caucasians.

Additionally, 20% of African Americans are uninsured while only 11% of Caucasians are without health insurance. Other modifiable personal factors affecting cancer control and detection include weight and diet, obesity, physical activity and exposure to some known environmental carcinogens (ACS-AA, 2007/2008).

There are increasing public health initiatives aimed at informing men about the risk of prostate cancer through community screenings. The ACS has sponsored programs to create change in public policy to help reduce health disparities among races. In addition, agencies such as the Centers for Disease Control and Prevention (CDC) have early detection programs that provide education and screenings. Many of these agencies work to reduce both modifiable and non-modifiable risk factors by educating men among races about the differences (ACS, 2009; ACS-AA, 2007/2008).

PSA-based Screening

Despite the considerable societal impact of prostate cancer, screening with the PSA serum test has raised considerable debate. There exists no standardized consensus within the medical community when weighing the benefits and harms associated with prostate cancer screening. Currently there are insufficient data linking screening with improved survival and therefore, no evidence suggesting that prostate screening should or should not be considered for low or average risk men and elderly men over age 75. Among men with low grade disease, opinions among clinicians vary out of concern over unnecessary biopsies, increased detection of possibly indolent cancers, dilemmas over treatment options, and uncertain complications of morbidity. In contrast, among men with aggressive disease, prostate cancer creates extensive societal anxiety to find a cure or

preventive measures while concerns loom over substantial resource consumptions that lead to high health care costs (Crawford & Abrahamsson, 2008).

The ACS recommends men of average risk receive both a PSA test and a DRE annually beginning at age 50. For men of higher risk (African Americans and men with strong family history) screening is recommended starting at age 45 years. The ACS-AA report noted that while having breast, cervical, and colon and rectum screening tests were not significantly different among African Americans compared to Caucasians in both males and females, use of screening tests among men for prostate cancer was clearly different for the 2004 year. For example, the Behavioral Risk Factor Surveillance System (BRFSS) of 2004 reported the proportion of women receiving a mammogram for breast screening was 59.4% and 58.6% among African Americans and Caucasians, respectively (see Table 2). The same survey noted the proportion of women receiving pap smears test for cervical cancer among African Americans and Caucasians to be 86.7% and 85.6% with screening for colon and rectum cancer at 19.2% and 19.4%. However, prostate screening using a PSA test was 50% and 55.4% and a DRE was 47.4% and 52.2% for African Americans and Caucasians, a relative percent difference of greater than 10% for both tests (50%/55.4% and 47.4%/52.2%). The survey noted no known reasons for the discrepancy in prostate screening use among races other than, perhaps, African American men's distrust in the medical community, lack of education about screening, and less likelihood of participating in community screening programs (Behavioral Risk Surveillance System, Public Use Data File, 2004).

Table 2. Percent Use of Cancer Screening Examinations, 2004.

Cancer Site	African American	Caucasian	Relative percent difference *
Breast			
Mammogram	59.4	58.6	1.3
Clinical breast exam (CBE)	64.3	65.6	-2.0
Mammogram and CBE	51.2	52.2	-1.9
Cervical			
Pap smear test	86.7	85.6	1.30
Colon and Rectum			
Fecal occult blood test (FOBT)	19.2	19.4	-1.0
Flexible Sigmoidoscopy	44.3	47.0	-6.0
Prostate			
Prostate Specific Antigen	50	55.4	-10.8
(PSA)	47.4	52.2	-10.1
Digital rectal exam (DRE)			

*negative value indicates percent fewer African Americans having tests. Source: Behavioral Risk Surveillance System, Public Use Data File, 2004.

Problem Statement

With final results from the European Randomized Screening for Prostate Cancer (ERSPC) and the Prostate, Lung, Colorectal, and Ovary Cancer Screening trial (PLCO) in the United States not yet available, researchers must rely on retrospective studies using observational datasets. The ERSPC and the PLCO trials are two randomized clinical trials that have closed however, continue to follow enrollees to evaluate the efficacy of prostate cancer screening with hopes of explaining differences in incidence and mortality rates, treatment strategies, and outcomes while addressing whether early prostate screening leads directly to saving lives. A randomized clinical trial has been described as the gold standard in most research areas. It involves the careful design of an experiment that ensures assignment of participants to treatment groups in a pure random fashion in

that assignment to groups is independent of the characteristics of the subjects and that the groups are similar in all other characteristics. The experiment is performed without biases. Because RCTs are carried out under these strict conditions, they are generally recognized as being internally valid. In contrast, because RCTs often exhibit results that are less than generalizable to the population, they can experience weak external validity. However, as valuable as RCTs may be, they are not without inherent limitations such as usually being conducted on highly selected patients in centers of excellence, under optimal strict protocol conditions, and sometimes costly and time consuming (Earle et al., 2001).

The decline in observed mortality rates for prostate cancer during the past decade suggests that early detection from increased screening and aggressive treatments may play a role. However, there remains no proven association. No national consensus regarding best practice patterns and screening patterns exist thus leaving the management of prostate cancer controversial (Harris & Lohr, 2002; Carter, 2007; AUA, 2009; ACS, 2009, 2010). Differences exist between African American men and Caucasian men regarding treatment strategies offered or chosen and in how they view screening programs that can result in different outcomes between these groups of men. These differences may result from African American men having less access to aggressive curative treatment, participating in fewer early detection screening programs, and possibly different risk and behavioral factors contributing to higher stage disease at diagnosis and worse overall prognosis. Available treatment options include surgery to remove the gland, radiation therapy including brachytherapy implants, hormone therapy

deprivation (ADT), and watchful waiting or active surveillance as it is sometimes called (ACS-AA, 2007/2008; Richert-Boe et al., 2003; Freedland & Isaacs, 2005; Jones, Shipp, Thompson & Davis, 2005; Marion & Schover, 2006).

Extensive studies exist using a multitude of secondary datasets evaluating screening habits and treatment management for prostate cancer. Even with community screenings and advanced technological treatments, differences have been reported among races. Most studies have shown conflicting and contrasting results or mixed outcomes at best. Often these studies consist of small sample sizes, fail to control for multiple factors that may confound treatment comparisons, and most do not show results from community practice.

In addition, the NCI has spent over $2 billion dollars on prostate cancer research. By the end of 2005 there were over 28,000 scientific papers published in peer-reviewed journals on prostate cancer. Advances have been made in regards to treatment, imaging, biopsy technology, screening tests, along with attempts to understand risk factors and disease, and in understanding behavioral issues (Roemeling & Schroder, 2006; Schmid, 2004; Carroll et al., 2001). Despite these recent advances, the frequency and variation of complications reported have differed. No emerging consensus exists regarding the optimal treatment for the most common cancer in men (AUA, 2009; Schmid et al., 2004; Draisma et al., 2004; Frankel, Smith, Donovan & Neal, 2003; Otto & deKoning, 2004). No uniform consensus exists regarding the efficacy of prostate screening and whether any beneficial effect that can be linked to reduced mortality. In fact, there are agencies that recommend screening and those who do not for various reasons. Some groups, such as

the American Urology Association (AUA) and the U.S. Preventive Services Task Force (USPSTF) suggest that prostate screening can be harmful with studies showing that PSA false positives may lead to unnecessary treatment and anxiety (AUA, 2009; USPSTF, 2008; Carter, 2007). Likewise, studies exist that show health disparities between African American and Caucasian men while others have not. A majority of these use population sizes from specific geographical regions making generalization improbable and robust power unlikely. Most studies use conventional statistical methods that are often filled with bias and multiple limitations (ACS, 2008, 2009; ACS-AA, 2007/2008; Harris & Lohr, 2002; Black, 2006).

In the absence of randomized clinical trial data and with the known limitations to resolve questions of whether early detection and aggressive treatment leads to decreased mortality rates in men with prostate cancer, use of the PSA test remains a subject of controversy. Therefore, researchers can only conduct studies using current observational data with analysis evaluated through traditional statistical methods to seek comparable outcomes to questions like why African American men have higher mortality rates than Caucasian men. And, if mortality rates are declining in both races, why then does a health disparity gap remain? Moreover, if conventional statistical methods continue resulting in mixed and variable resolutions to these unanswered questions, then additional statistical methods should be considered. Various limitations exist when performing retrospective observational studies. Confounders are difficult to account for due to lack of randomization and inherent selection bias that often lead to mixed results.

This study seeks to expand on previous research providing new information by exploring use of the PSA test as a screening tool to gain knowledge and better understanding of its relationship to disparate mortality rates among elderly African American and Caucasian men. Men become Medicare eligible beginning at age 65; however, men aged 66 and over are included in this study because the median age of men diagnosed with prostate cancer is 68 with almost 64% of prostate cancer diagnosed in men over 66. Including men aged 66 instead of 65 also provides a full year of Medicare claims data to assess comorbidities. A secondary aim will be to explore PSA utilization rates among race for the group of men diagnosed with localized/regional prostate cancer and from the group of men without prostate cancer. A 5% randomized sample of non-cancer cases are provided in the SEER-Medicare dataset and will be used to develop population-based estimates of use of the PSA test throughout the study period. Figure 3 represents an illustrative model for the groups, the treatment (binary intervention), and the outcome for the study. The solid lines indicate the direction of the primary goal of examining screening PSA tests (treatment intervention) and its effectiveness on disparate mortality rates among race from the group of men with prostate cancer. Additionally, the study will be repeated comparing men receiving screening PSA tests (treatment intervention) and its effectiveness on overall mortality among race in men who do not have prostate cancer. Finally, the dashed lines show the path of the secondary aim which is to analyze PSA utilization rates among race from the group of men with prostate cancer as well as utilization rates for race from the group of men with no cancer.

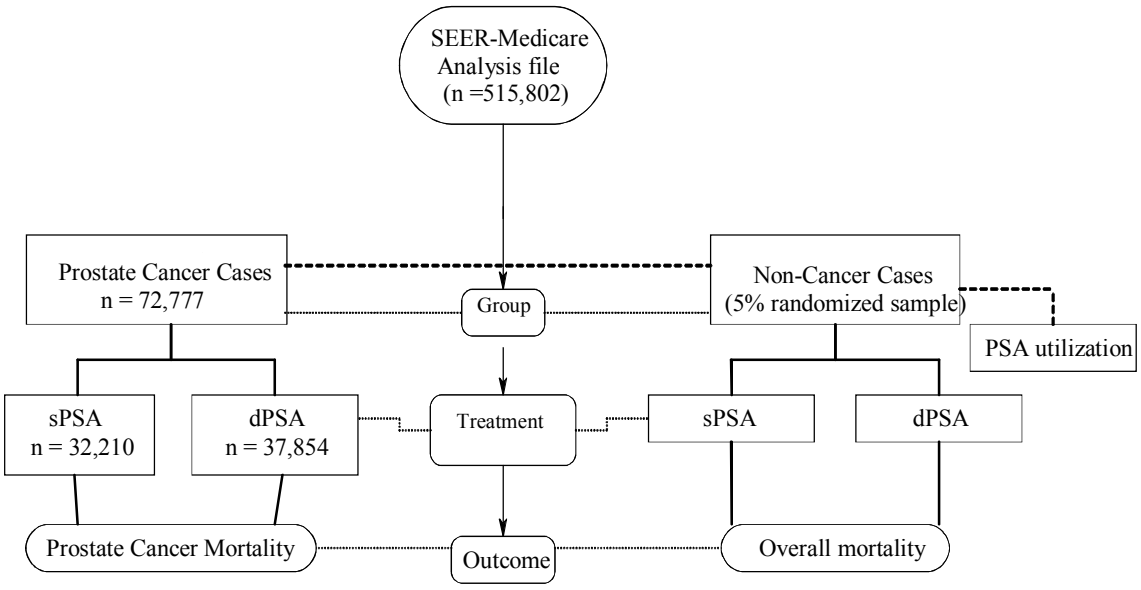

Figure 3. Illustrative model of groups, treatment intervention (screening PSA), and outcome.

Evaluation of this research study will be a multi-stage process. Baseline, summary, and descriptive statistics will be provided for the categorical independent variables and tests for differences in means will be assessed for the continuous independent variables. Initial logistic regression models will be created to assess variance among independent variables for screening versus non screening and among race. These initial logistic models will be compared to other logistic and Cox regression models once a propensity analysis has been applied and men matched and paired.

The distributional variance of covariates will be examined for differences and balance among race within each of the five quintiles within the treatment group (screening PSA) and the control group (no screening PSA). Balance of covariates will be assessed by quality assessment tools presented in chapter three using various graphical

plots. After generating initial logistic regression models, a propensity analysis using logistic regression with the intervention (sPSA) as the dependent variable will be performed. The propensity analysis provides the estimated propensity scores (p-score) for all independent variables. The p-score is defined as the probability of a man having a screening PSA test based on the baseline characteristics. The regression model will yield estimates of this probability and will range from 0-1. Following this analysis, all men will be matched, paired, and placed into strata of five quintiles based on their p-scores. Assessment of whether the p-score helped to balance the covariates can then be performed by again, examining differences in racial groups within quintiles and notation of the adjusted p-value provided in the propensity logistic model (in this case, a p-value > 0.05 would show no significant differences between covariates and therefore indicate balance has been achieved). Further assessment of covariate distributions within each quintile may show the inability to detect differences after p-score adjustment. For example, the initial regression model should indicate sufficient overlap of covariates by showing no extensive or consistent patterns of interactions between screening PSA and each quintile. This would allow for including the p-score as a covariate in all subsequent regression models to explicitly account for most of the selection bias. Should assessment of overlap prove sufficient, a final propensity score adjusted logistic regression and conditional Cox regression model will be developed for group comparisons. A final statistical analysis will be performed using both regression models for examining main treatment effects that independent variables, including p-scores, have on the dichotomized outcome response variable mortality.

Propensity scoring analysis is helpful for removing selection bias by balancing groups on all observed variables thus allowing placement of men into quintiles of which conventional statistical methods can then be applied. This method provides a means of achieving randomization in descriptive observational studies. Propensity scoring analysis also increases statistical power and aids in further improving overall generalization similar to that of randomized clinical trials (Rosenbaum & Rubin, 1983; Love, 2003; D'Agostino, 1998). Multivariate matching and stratifying are also helpful when trying to control confounders that cause bias. An advantage to these methods is the effect of multiple other factors can be controlled for at the same time (Grimes & Schulz, 2002).

A large database compiled from SEER-Medicare linked files will help to ensure external validity by providing greater generalization to the national population. The SEER Medicare linked files are population-based where incidence data for individuals are linked to their mortality data therefore making it possible to examine mortality by using variables determined at the time of diagnosis, such as PSA screening. The NCI defines this as incidence-based mortality (IBM).

Purpose

The purpose of this study is to extend previous research and provide new information for effectively identifying PSA screening's influence on disparate mortality between African American and Caucasian men who have and who do not have localized prostate cancer. The secondary dataset used are merged SEER-Medicare files from 1986 through 2006. The primary aim of the research is to conduct an analysis of prostate screening with PSA and its effect on racial disparate mortality among a group of men

with prostate cancer and repeated for a group of men without cancer using the latest SEER-Medicare dataset and a relatively new statistical method in the propensity scoring method. Once propensity scores are determined and shown to have sufficient overlap, that is, selection bias has been removed; groups can be matched and placed into quintiles. Subsequent multivariate logistic regression analysis will be performed. Finally, a main effects logistic and conditional Cox regression model will be developed demonstrating the greatest association between independent variables and the outcome response variable of mortality.

The same analysis will occur for the non-cancer cases to examine if differences exist in overall mortality between races in men without prostate cancer. Knowing whether mortality rates among race differ in men without prostate cancer could produce clues for the presence of any unobserved variables and help explain bias effects in mortality differences in men with prostate cancer. For example, if differences are established in one group and not the other, then other factors (unobserved variables) could be involved calling into question the reliability of using mortality as an endpoint to assess screening efficacy in nonrandomized studies. This is reasoned by the notion that any realized health benefit from screening PSA (early detection) would be evident only through differences in prostate cancer-specific mortality but should differences appear in overall mortality (men without prostate cancer) then selection bias would be playing a greater role and should lead the way for further exploration.

Given the controversy surrounding unproven survival benefits, harms, and screening guidelines of prostate screening, a secondary aim will be to evaluate PSA

utilization rates over a two period era, the PSA era and the post-PSA era. The study period of 1986-1995 will serve as the PSA era and the period of 1996-2006 as the post-PSA era. Among groups, those men diagnosed with prostate cancer and those without cancer but who received regular screening will be evaluated by test of proportions for the two periods. Should factors be identified showing differences between African American men and Caucasian men regarding screening habits and mortality then new race-based public policy prevention mechanisms could be examined. Hope lies with randomized clinical trials for proving that PSA screening for early detection and prevention can lead to reduced mortality rates and narrowing the disparity gap among races. Until then, observational studies using secondary data sets are warranted. The strengths of this study are use of the most recent SEER-Medicare data and a propensity scoring methodology, which is generally regarded as robust and accurate, subject to fewer restrictions, and enables improved confounder accountability (Rosenbaum & Rubin, 1983; Love, 2003; Grimes & Schulz, 2002).

Research Questions

1. Are men **with** prostate cancer equally likely to have similar prostate cancer-specific mortality rates among race for screening PSA tests compared with diagnostic PSA tests?

2. Are men **without** prostate cancer equally likely to have similar overall mortality rates among race for screening PSA tests compared with diagnostic PSA tests?

3. Did baseline (initial) PSA screening rates differ among men **with** prostate cancer during two eras, the PSA era 1986-1995 and the post-PSA era 1996-2006?

4. Did baseline (initial) PSA screening rates differ among men **without** prostate cancer during two eras, the PSA era 1986-1995 and the post-PSA era 1996-2006?

Based on the overview presented, the following hypotheses are provided regarding the extent that screening has on disparate mortality rates among African American and Caucasian men with prostate cancer.

Hypotheses

H_1: No statistically significant differences exist in prostate cancer-specific mortality rates among race for men with PSA screen detected cancer and men with clinically diagnosed cancer,

H_2: No statistically significant differences exist in overall mortality rates among race for men *without* prostate cancer receiving screening PSA tests and men receiving diagnostic PSA tests,

H_3: The baseline (initial) PSA screening rates among race in men *with* prostate cancer in the two PSA eras from 1986-2006 will show no statistically significant differences,

H_4: The baseline (initial) PSA screening rates among race in men *without* prostate cancer in the two PSA eras from 1986-2006 will show no statistically significant differences.

Significance of the Study

The outcome of this study is to understand the disparate relationship in mortality among African American and Caucasian men with localized prostate cancer. This observational retrospective study may guide future research in developing treatment regimens formulated from race-based PSA guidelines and unique to the individual patient based on improved knowledge and understanding of the complex factors associated with racial disparate mortality rates. Furthermore, the current study may become a surrogate or complement to time consuming and costly prospective randomized clinical trials. The study will also provide more objective clinical data in order that shared decision making

among physicians and patients concerning screening practices will be clearer. The study will generate debate of whether the PSA test should ever be used as a screening tool for a cohort of elderly men with and without localized/regional prostate cancer thus having a major impact on the validity of the PSA test itself. Using a robust statistical analysis such as the propensity scoring method along with one of the most recent population based secondary datasets could help shape public policy toward establishing race-based screening guidelines for improved prostate screening programs.

Data and Analysis

The study is a retrospective observational design analyzing data from the 1986-2006 SEER-Medicare linked datasets (National Cancer Institute). Prostate cancer patients diagnosed from January 1, 1986 through December 31, 2006 (n = 515,802 cases) whose data were entered into the linked databases are included. Surveillance, Epidemiology, and end Results (SEER) cancer registry data merged with Medicare health care claims provide linked patient demographic information, initial PSA testing and diagnostic information, initial treatment, and long-term follow-up status of national cancer incidence and mortality rates making the data suitable for health services research (Warren, Klabunde, Schrag, Bach, & Riley, 2002). The latest release of SEER-Medicare linked data includes cases diagnosed through 2006 from all regions except Alaska and the Arizona Indians and Medicare claims data through 2005.

The SEER Medicare linked database is sponsored by the National Cancer Institute and combines clinical information from population-based cancer registries with claims information from the Medicare program. Since initial data collection began in 1973, the

number of registries has expanded and now includes approximately 26% of the U.S. population. The SEER data are considered highly valid with quality and completeness studies performed yearly to ensure accuracy by holding the highest level of certification of quality as provided by the National American Association of Central Cancer Registries. The program's standard for completeness of data ascertainment is 98% (Warren et al., 2002).

Summary

Prostate cancer is the second leading cause of cancer death among men in the U.S. with over 2.6 million men diagnosed and almost 375,000 deaths occurring since 1995 (AUA, 2007). However, because of improved treatment technologies and possibly from early detection, mortality rates for the disease have been declining since that time with 34,475 men dying in 1995 compared with more than 27,300 deaths estimated for 2009 (AUA, 2007; ACS, 2009).

Many studies have shown improved outcomes due to advances in treatment regimens, prostate imaging, biopsy methodology, in understanding risks, education, and public awareness. However, there still remains no consensus for optimal screening patterns, screening intervals, and screening tests that might lead to best practice guidelines for early stage disease. Furthermore, there have been few studies that evaluated race-based policy concerning screening with PSA to help in understanding the mortality differences in African American and Caucasian men. This study examines several variables to determine the extent to which they might contribute to the racial

disparate mortality rates observed among African American and Caucasian men when considering PSA utilization.

The study will incorporate a robust, statistical method in the propensity analysis that has not yet been applied to evaluations of race-based mortality differences and screening PSA tests alone. The propensity method will allow for matched groups on observed variables in order to simulate randomization. This method together with the most update and complete dataset of the National Cancer Institute's SEER-Medicare merged file system will advance not only perceptions of screening efficacy for prostate cancer, but also it will increase clinical knowledge of the disease by identifying, quantifying, and analyzing variables and correlating them to the value of the PSA test to determine if their presence, absence, or variance might explain disparate mortality rates among African American and Caucasian men. Results may help guide public policy toward more individualized race-based screening guidelines and provide physicians with new information about ways to communicate screening tests that may be best for individuals.

Organization of Dissertation

The literature review in the following chapter includes an overview of prostate cancer in the U.S. and describes relationships between screening and mortality rates among African American and Caucasian elderly men. It includes discussion of various screening studies along with current guidelines, available screening tests, and observed mortality among races. Chapter 3, entitled Methods begins with a brief examination of the theory of the propensity scoring method and its applications to health services

research along with sample graphical assessment tools. A description of the analytical strategies employed in the study, including data source, sample population, methods, study variables, and hypothesis testing are provided along with discussions of the study limitations. Chapter 4, Results will present and briefly discuss findings. Chapter 5, Discussion, will address results, limitations of the study, and implications for public health policy and future health services research.

CHAPTER 2: LITERATURE REVIEW

The purpose of this review is to summarize literature concerning PSA use in men with prostate cancer and subsequent outcomes associated with African American and Caucasian men. The chapter begins with a discussion of prostate cancer followed by a brief discussion of prostate screening utilization in the United States including the PSA test and screening guidelines. This is then followed by a more extensive discussion of prostate screening studies including initial evaluations from two large population-based randomized clinical trials (RCTs) of the European Randomized Screening Prostate Cancer in Europe and the Prostate, Lung, Colorectal, and Ovarian trial in the U.S. Also discussed are factors associated with cancer specific mortality and risks of prostate cancer. Lastly a summary of the literature reviewed for this study is provided.

Much of the research focusing on prostate cancer emphasizes screening controversies, treatment strategies, and outcomes issues within the U.S. and internationally. Other research focuses on barriers associated with access, social-behavioral relationships, and racial disparities observed in screening programs, treatment choices, and outcomes across ethnic groups. Most studies are retrospective in design and use secondary datasets mainly because complete results from randomized clinical trials are small in number or not yet available due to numerous years of follow-up required before statistical inferences can be made.

Prostate Cancer

Prostate cancer is a malignant disease that begins growing within the prostate gland. It is the most common cancer diagnosed in American men with 192,280 new cases and 27,360 deaths estimated for 2009 (ACS, 2009; ACS-AA, 2007/2008). Since 1995, 2,600,000 men in the U.S. have been diagnosed with prostate cancer and almost 375,000 have died from the disease (AUA, 2007). Autopsies have shown that about 15-30% of men over age 50 have microscopic cancerous cells present. By age 80 the percent rises to 60-70% of men. In addition, a newborn boy has a 16% chance of developing prostate cancer in his life time but only a 3% chance of dying from the disease (Carter, 2007).

Cancer is a disease characterized by the uncontrolled growth of cells having the potential to spread or metastasize to other parts of the body. Normally, cells divide with regularity in order to sustain life. However, when cells grow abnormally and at uncontrolled rates they become masses known as tumors. Some tumors are malignant (cancerous) and others are benign (non-malignant). Sometimes the growth of benign prostate tumors can interfere with normal bodily functions such as urinating; however, they are seldom life threatening. Any time the prostate gland enlarges, men experience urinary symptoms such as nocturia (nighttime urination) and increased urgency and frequency (the need to urinate more often). These symptoms can be mistaken for a common condition known as benign prostatic hyperplasia (BPH). BPH occurs when the tissue of the transition zone grows or swells causing stricture of the urethra that can lead to urinary problems (Carter, 2007). However, these same symptoms may also be experienced in men with early stage localized disease as well.

In early stage prostate cancer, men typically experience minimal or no symptoms when the tumor remains localized within the gland and has not yet invaded or extended through the capsule surrounding the gland. On the other hand, if cells of malignant tumors spread beyond the prostate capsule and enter the bloodstream or lymphatic system they may eventually invade and destroy normal tissues and organs at distant sites. When this occurs, new tumors are formed in those areas which eventually lead to symptoms and problems. Many men often experience erectile dysfunction or loss of penile firmness when prostate cancer has spread to the nerves that control erections. Unfortunately, usually once prostate cancer has spread to lymph nodes, bones, or other organs, many men experience pain in the pelvic region, hips, back, ribs, and other bones (Carter, 2007; TAP Pharmaceuticals, 2003).

The natural history of prostate cancer is not well understood, and as mentioned earlier, most men die **with** rather than **from** prostate cancer. A recent Lancet report noted that of patients who had their prostate cancers found through screening and ones that may not evolve into life threatening disease or reduced quality of life, only 16% would benefit from aggressive treatment. This implies that the remaining 84% receiving aggressive treatment would not benefit (Frankel et al., 2003).

Prostate Screening

PSA Evolution and Screening

In 1986 the Food and Drug Administration (FDA) first approved use of serum PSA in the U.S. for testing recurrence of prostate cancer. PSA was not initially intended as an early detection tool for screening. However, as a result of its ease of measurement

and minimal invasiveness, rapid dissemination of the PSA test as an early screening test increased in the U.S. from the late 1980s through 1990. Since that date, use of the PSA test to detect cancer has been debated, scrutinized, contradicted, and contrasted by multiple case-finding studies throughout the world. Normal levels of PSA found in the blood varies with each individual, ideally ranging from zero to less than 4.0 ng/ml; however, today in the U.S. a threshold value of 4.0 ng/ml is the accepted minimum value that would trigger further diagnostic work up.

Although the question of whether to use the PSA test for prostate screening remains unanswered and is one of the most controversial and debated topics in medicine today, one important clinical finding of the PSA test, or any screening test for that matter, must be its ability to differentiate cancer from benign disease (Roemeling & Schroder, 2006; Schmid, 2004; Carroll et al., 2001). Opponents argue against screening with the PSA test for several reasons, including its unproven effectiveness to reduce prostate cancer-specific mortality, the unknown risks and benefits regarding the psychological effects of additional unnecessary testing such as biopsies, and the increased risk of overdetection and unnecessary side effects of aggressive treatment (Schmid, 2004; Draisma et al., 2004; Frankel et al., 2003; Otto & DeKoning, 2004).

Although it is widely believed that early detection and aggressive treatment may reduce incidence and mortality rates for some cancers, it remains unclear whether prostate screening is useful for early detection and whether it is linked to increased cure rates and prevention without confirmation by randomized clinical trials. These were some of the concerns surrounding the creation of an international cooperative led by multiple

European countries to form the European Randomized Screening for Prostate Cancer Trial (ERSPC) and the Prostate, Lung, Colorectal, and Ovarian (PLCO) trial in the U.S.

An Austrian study using data collected by the ERSPC trial examined the effect of PSA screening on mortality in the city of Tyrol, Austria. The city of Tyrol had no particular screening guideline other than the PSA which was offered free of charge. PSA was received by 100% of the eligible male population. The authors compared mortality rates from Tyrol with other cities within Austria that either did not offer prostate screening or did for a minimum cost. The study noted that PSA screening utilization was used in 5.1% of all newly diagnosed cases in 1984 with the utilization rate rising to 60.6% by 1994 (Bartsch et al., 2001). Bartsch and colleagues (2001) reported that using PSA screening for early detection showed a significant down-staging of disease leading to more successful aggressive treatments in Tyrol. Of the 307,249 men living in the Alpine region of western Austria during 1993, 65,123 (21%) of them between the age of 45 and 75 were advised and encouraged to undergo a PSA test. No significant differences were noted between the trends in Tyrol and the rest of Austria before 1993. However, a decrease in mortality was reported in Tyrol after 1993 ($\chi^2 = 12.74$, df = 1, p = 0.0004) where the log mortality rate decreased at a rate of 0.092 (SE 0.024) per year from 1993 onward.

The results of this study showed that when PSA screening was offered to a population-based environment free of charge and where utilization rates increased by almost 12 fold over ten years, mortality was reduced. The authors believed the results were as expected because the screening was performed in a uniformly available and free

testing program where a large proportion of men were screened. Race or ethnicity was not considered as a factor for PSA screening differences for this study (Bartsch et al., 2001). The authors concluded that while it is likely that programs offering PSA testing in support of early detection may contribute to a decline in mortality, they acknowledged that their study did not support such a statement. They believed that further research into the PSA and DRE test would be necessary.

A PSA test and a DRE are the common tests performed at community screenings mainly because of their ease of measurement and non-invasiveness. However, not enough evidence has been produced regarding the efficacy of both, whether used together or separately, the PSA and DRE still remain controversial and as a result guidelines on screening have varied (Coldman, Phillips & Pickles, 2003; Weinmann, Richert-Boe, Glass & Weiss, 2004). Despite the controversy and uncertainty surrounding the use of prostate screening and screening guidelines, the American Cancer Society for African Americans reported that during 2004, 50% of African American men aged 50 or older had a PSA test and 47.4% had a DRE exam within the past year compared to 55.4% and 52.2% for Caucasian men (ACS-AA, 2007/2008). The report did not mention why the year 2004 was the single year analyzed. It may have been because of known costs and length of time required for following cohorts longitudinally (Altman, 1999).

When being screened for prostate cancer, men can be divided into various groups; 1) screen detected men with prostate cancer but who would have never become symptomatic and whose outcome would not be affected by aggressive treatment in their lifetime (overdetection); 2) screen detected men with curable early stage prostate cancer

that would not have been clinically diagnosed until distant metastasis occurred thus screening would have improved their outcome; and 3) screen detected men with prostate cancer and diagnosed at the same stage as if diagnosed by clinical methods and who would benefit from treatment (see Table 3).

Table 3. List of Men Benefiting from Prostate Screening.

	Screen detected prostate cancer	Symptomatic	Outcome affected by treatment	Distant metastasis	Would benefit from screening
Men of group 1	Yes	No	No	No	No
Men of group 2	Yes	No	Yes	Yes	Yes
Men of group 3	Yes	Likely	Yes	No	No

The first group would die with indolent prostate cancer and should have never been screened. The second group would benefit the most from screening and would most likely contribute to real reductions in mortality rates. The third group should not have been screened because they were likely symptomatic at the time of screening and thus should have been categorized as clinically diagnosed instead (Frankel et al., 2003; Roemeling & Schroder, 2006).

However, if men are screened and disease is detected at early stages, they will most likely benefit from aggressive treatment as 5-year survival rates during the late 1980s and early 1990s (initial PSA utilization periods) were between 75-85% among all races (ACS, 2008; ACS-AA, 2007/2008; Carter, 2007). Transitioning through the 1996 -

2004 period (later PSA utilization periods), the race-based 5-year survival rates for African Americans and Caucasians were reported as 96% and 99%, respectively. Finally, further improvements were made as current 5-year survival rates are 98.9% for all stages and 100% for localized disease for men of all races (ACS, 2009). Although survival rates have improved for various reasons, including the possible contribution from early detection by screening, there is little evidence that PSA screening has led to reduced cancer specific mortality in these men (ACS, 2008; ACS, 2009; Challen, 1998; Gottlieb, 2003; Roemeling & Schroder, 2006; Harris & Lohr, 2002). In fact, it has been suggested that if threshold values for the PSA test (currently accepted as 4.0 ng/ml in the U.S.) were lowered in order to detect even earlier stage disease in younger men, overdetection rates (false positives) would increase and subject some men to increased anxiety, more positive biopsies, and aggressive treatments that may lead to the unnecessary harmful effects of incontinence, impotence, and bowel problems. In contrast, it has been suggested that the PSA threshold value be raised for the elderly where PSA levels rise naturally in men of that group anyway (Gottlieb, 2003; Frankel, 2003; Roemeling & Schroder, 2006; Carroll et al., 2001).

Furthermore, it has been suggested that the PSA test is ineffective and inaccurate since results frequently vary between multiple tests for the same patient. Yet, most of the medical community continues to offer that men with varying results undergo additional invasive testing and expensive treatments which can cause complications and lead to unnecessary distress, anxiety, and poor health related quality of life issues. For example, urinary and sexual dysfunctions are associated with surgical procedures such as

prostatectomy whereas bowel complications are associated with radiation therapy treatments. Of these complications, sexual dysfunction has the greatest association with a man's perception of how well his cancer was managed, perceptions of masculinity, and self-confidence (Douglas, 2007; Dale, Bilir, Han & Meltzer, 2005; Otto & DeKoning, 2004).

Moreover, only 15% of men with PSA results less than the normally accepted value in the U.S. of 4.0 ng/ml will have prostate cancer, and only 2% of those will have advanced high grade disease. These conflicting results have likely helped to generate a nearly universally accepted consensus that thresholds may be impossible to achieve (National Comprehensive Cancer Network [NCCN], 2008; Carroll, 2001). Therefore, the current U.S. threshold limit of 4.0 ng/ml itself is unsubstantiated as it has been shown that up to two thirds of cancers can be missed at this level. Further, early results from the ERSPC trial found that among the men with PSA levels less than 4.0 ng/ml cancer detection rates of 36.5% were identified (Frankel et al., 2003). Moreover, because the ERSPC had not substantiated a threshold level prior to 1997 and because fear existed among researchers that too many cancers would go undiagnosed, the ERSPC decided to lower its threshold level to 3 ng/ml in early 1997 (Otto & DeKoning, 2004). So there may be an indication for re-evaluating current PSA threshold values, even the possibility of setting values based on age or race instead.

Screening Guidelines

Screening for disease has become part of contemporary medicine and already normal practice for cancers like breast, cervical, colorectal, lung, and ovarian. The

rationale for population or community screenings is straight forward: use of sensitive and specific screening tests with the ability to detect asymptomatic cancers in their earliest stage in order to provide treatments that can cure the disease. Often it is difficult to determine whether men participate in community screening programs because they believe it to be a preventive measure and beneficial to their health or because they are symptomatic and wish to confirm the presence of disease by further diagnostic work up.

Guidelines for prostate screening have been controversial and debated for years. Bostwick and colleagues (2004) reported that in the United States, the lifetime risk of a man dying **from** prostate cancer is only 3%, whereas the risk of dying **with** prostate cancer is approximately 72% (Bostwick et al. 2004; Giri et al., 2007). However, most authorities agree that men at increased risk for prostate cancer may have more aggressive disease and would therefore benefit from screening and treatment. Most organizations recommend screening beginning at age 40 to 45 for men at increased risk. High risk men are generally defined as African Americans and those men with a family history of prostate cancer (Grubb, Roehl, Antenor & Catalona, 2005; Giri et al., 2007; ACS, 2009; AUA, 2009; NCCN, 2008).

Screening guidelines vary among the majority of leading health care agencies with the most common variations occurring in the initial age recommended for screening, the definition of risk factors, and the potential harms and benefits from screening and are listed later in the chapter. In general, the American Cancer Society and the American Cancer Society for African Americans recommend baseline screening using both the PSA test and a DRE in men 50 years of age and who have a life expectancy of at least 10

years. The American Urological Association recently released its latest **New PSA Best Practice Statement: 2009 Update** (AUA, 2009) revising its original position that followed the American Cancer Society and instead now recommends that all men have a baseline PSA and DRE at age 40. The AUA further recommends that only well-informed men who wish to pursue early diagnosis be offered a PSA test. A well-informed man is one who has communicated and fully understands the information provided by his physician on topics of risks and benefits of screening, of all treatment options (including active surveillance), has been provided with a pre-treatment individualized risk assessment, and post-treatment monitoring. Lastly, the AUA now does not recommend a single PSA threshold value be used to prompt a biopsy. In addition, the National Comprehensive Cancer Network (NCCN) along with both the ACS and the AUA recommends considering biopsy beginning at age 45 in men who had PSA test results greater than 2.5 ng/ml and in all men of high risk. The MD Anderson Cancer Center in Houston, Texas recommends all men, including those of high risk and African Americans begin at age 45 with a baseline PSA and annual tests thereafter. In men of ages 50-74, MD Anderson recommends using both the PSA and DRE but suggests consideration be given on issues of ethnicity, family history, comorbid conditions, life expectancy, and results from previous testing. Memorial Sloan-Kettering Cancer Center of New York recommends men have both a PSA and DRE at age 50 and African Americans and high risk men begin screening at age 40.

In contrast, the U.S. Preventive Services Task Force, the American College of Physicians, and the Canadian Task Force on the Periodic Health Examination have

concluded that evidence is lacking on whether benefits of prostate screening outweigh the harm. Therefore, they make no recommendations for routine screening in asymptomatic men younger than 75 and caution that risks and costs of potential harm may outweigh benefits of screening (Weinmann et al., 2005). For men age 75 and older with a life expectancy of 10 years or less, they have suggested that the incremental benefit from treatment of prostate cancer detected by screening is minimal: "the harms outweigh the benefits and that screening should not take place" (Weinmann, et al., 2005, pg. 367).

Some groups, such as the U.S. Preventive Services Task Force suggest that physicians should describe and discuss potential benefits and harms associated with prostate screening, explain diagnosis and treatment options, and inform patients of the lack of evidence of the benefits of screening. As a result, these groups propose that an individual's personal preference should take precedence in guiding the shared-decision making of patients and their physicians on screening (Bunting, 2002; Calonge et al., 2008). Unfortunately, controversial guidelines could make physicians reluctant to follow any guidelines and thus recommend their own specialty as the appropriate treatment choice. For example, urologists may suggest surgery or watchful waiting and radiation oncologists may suggest radiation therapy with neither offering the patient counsel by the other professional provider which therefore, could preclude the patient from having complete information to make informed decisions.

The poor specificity of PSA testing increases the likelihood of false positive results that can lead to unnecessary prostate biopsies and emotional distress. Researchers have attempted to improve specificity by using age-adjusted PSA values or free-to-total

serum PSA ratios (percent free PSA) as indicators of cancer (Carroll, 2001; AUA, 2009; Carter, 2007). The free/total PSA ratio or percent free PSA is defined as the ratio of the amount of unbound PSA (free) in the blood to the total amount of PSA in the blood as serum PSA exists in two forms; one bound to plasma proteins and one in a free state (Carroll, 2001). Age-adjusted PSA values, as recommended by physicians for young men and men of high risk, may need to range from 0-2.0 ng/ml for ages up to 49 years, 0-4.0ng/ml for men 50-59 years, 0-4.5 ng/ml for men of 60-69 years, and 0-5.5 ng/ml for men over 70 years (Carroll, 2001).

Ambiguous results and controversial experiences noted above point to the need for randomized clinical trials to address the effectiveness of prostate screening to reduce mortality. However, some researchers believe that beneficial results from a RCT may be difficult to obtain or even unlikely if contamination occurs within control arms (Otto & Roobol, 2006). Contamination bias occurs when men within control groups (no screening) of randomized clinical trials have had previous PSA tests performed (before inclusion into RCT) and who elect to participate simply to confirm presence of disease. Therefore, there continues to be controversy surrounding the effectiveness of current prostate screening tools. The various agents that lead to the controversial debate on screening guidelines are listed later in the section.

Screening Studies

A summary of screening studies are listed later in this section. A recent comprehensive review of the literature conducted by the Prostate Cancer Prevention Trial (PCPT) examined the performance of screening for multiple cancers, including prostate.

The study acquired reviews based on sensitivity and specificity of screening tests, the positive predictive value of screening tests, the number of men needed to screen (NNS) in order to detect one case, and the cost per quality-adjusted life-year (QALY) used for various screening programs. For the PSA test, the Prostate Cancer Prevention Trial (Crawford & Abrahamsson, 2008) reported a direct linear relation for the risk of positive biopsy and risk of high-grade disease with an increasing PSA test. The PCPT also noted that there was no justification in using a PSA value of 4.0 ng/ml as a threshold for detecting prostate cancer all of which contribute to the debate on screening guideline discrepancies (see Table 4). In particular, the report noted that a PSA value of 2.6 ng/ml had a sensitivity of 40.5% and a specificity of 81.1% for detecting cancer, whereas a PSA value of 4.1 ng/ml had a sensitivity and specificity of 20.5% and 93.8%. In other words, sensitivity to detect prostate cancer decreases and specificity increases with rising PSA. Overall, the PSA test proved a better tumor marker for advanced stage disease rather than for early stage disease.

Although the sensitivity of the PSA test to detect prostate cancer is low compared with other cancer detection tools, specificity for the test remains high. So then, high specificity of the PSA test begs whether correctly identified cancer cases through detection will ever be clinically significant to the patient. Basically, is prostate screening associated with reduced mortality (Crawford & Abrahamsson, 2008)? The PCPT report acknowledged that although the sensitivity/specificity profile was not perfect, it could still be useful when measured more than once and over time. It is important to note that

Table 4. Summary of Screening Guidelines from Various Health Care Organizations.

Medical organizations	Initial evaluation
American Cancer Society American Cancer Society for African Americans	Offer PSA and DRE beginning at age 50 in men with life expectancy greater than 10 years. For African Americans and those with family history beginning at age 45. Provide information about potential benefits/harms associated with screening
AUA New PSA best practice statement: 2009 update	Recommend for well-informed men wishing to pursue early diagnosis Age lowered to 40 for all men Discussions of risk vs. benefits, treatment options, pre-treatment individualized risk assessment, post-treatment monitoring No longer recommends a single threshold value that would prompt biopsy
American Academy of Family Physicians American College of Physicians American College of Preventive Medicine American Medical Association	Offer PSA and DRE beginning at age 50 in men with life expectancy greater than 10 years. Discuss potential benefits/harms, consider patient preferences, and share in decision making.
U.S. Preventive Services Task Force Canadian Task Force International Cancer Union (UICC) World Health Organization (WHO)	Men younger than 75 years and < 10 yr. expected life - No recommendation due to insufficient evidence Men ≥ 75 years – do not screen because there is moderate to high certainty of no screening benefit or harms outweigh benefits. Discuss potential benefits/harms, consider patient preferences, and share in decision making.
MD Anderson Cancer Center, Houston Texas	Consider baseline PSA in men at age 45. Annual PSA and DRE in men 50-74 years & age 45 for African Americans and men with family history.
Memorial Sloan-Kettering Cancer Center, New York	Annual PSA and DRE men beginning at age 50. African Americans and men with family history beginning at age 40.

cancers not detected by an initial PSA test could most likely be detected by a second test at a later time, conceding that delays in measurement would most likely not cause the disease to progress to non-curable stages (Crawford & Abrahamsson, 2008).

A recent update on the evidence of PSA use conducted for the U.S. Preventive Services Task Force (USPSTF) with assistance from the Research Triangle Institute-University of North Carolina Evidence-Based Practice Center examined key research publications (Harris & Lohr, 2002). The USPSTF reviewed literature looking for indirect evidence relating improved mortality and PSA screening based on 8 key themes. These included questions on the efficacy of 1) screening, 2) yield of screening, 3) surgery, 4) radiation therapy, 5) androgen hormone deprivation, 6) watchful waiting, 7) harms of treatment, and 8) cost and cost effectiveness of treatment (Harris & Lohr, 2002). The study examined relevant search terms from the MEDLINE database and the Cochrane Library for publications from January 1994 through September 2002. All articles were abstracted by the first author, and one trained assistant.

Within the first theme, **efficacy of screening**, Harris and Lohr (2002) found one randomized clinical trial dealing with efficacy of prostate screening conducted in 1988 in Quebec City. A sample of 46,000 men was randomized into two groups: one group invited to receive a PSA and DRE test and a control group not invited to receive the tests. Twenty three percent of the invited group and 6.5% of the non-invited group received a PSA and DRE test. After 8 years of follow up, study results indicated no differences in prostate cancer death rates between the groups (4.6 vs. 4.8 deaths per 100,000 men) (Harris & Lohr, 2002).

An extension of this 1988 Quebec study was conducted from the Laval University Prostate Cancer Screening Program (LUPCSP) extending the 8 year follow up out to 11 years (Labrie et.al, 2004). This study reported findings after 11 years of total follow up and again only noted a 23.6% response rate. The results indicated that 74 men died of prostate cancer out of a sample of 14, 321 unscreened controls and 10 deaths occurred in the screened group of 7, 348 men (Labrie et al., 2004). The study involved men aged 45-80 years that were randomized into screening and non-screening groups and included both a PSA and a DRE, with a threshold value of 3.0 ng/ml as the upper limit for a normal PSA. Labrie and colleagues (2004) reported an annual prostate cancer-specific death rate during the 11 year period from November 15, 1988 through December 31, 1999 as 19.8 and 52.3 per 100,000 man-years in the screened and non-screened groups respectively. This is equivalent to a 62% reduction in mortality in the screened versus non-screened group (two-sided p value < 0.002, Fisher's exact test). Results were expressed as events per 100,000 man-years in order to account for the specific years of exposure for each man in each group. The report noted that **age** and whether a man was **screened** or **unscreened** were the only significant explanatory variables in the study. Dummy variables created for the residential locations of men within the areas of Quebec City had no effect on the results, however **age** and **screened** versus **unscreened** had a highly significant effect ($p = 0.0054$ and $p = 0.0025$ respectively). The study did not mention whether ethnic groups were evaluated. In addition, contamination rates within the control group were not assessed with reasons not listed (Labrie et al., 2004). Furthermore, because of the low response rate for men randomized to receive a PSA test

(23.6%), the Quebec study's susceptibility bias was high. Susceptibility bias is created when small numbers of participants are reported (Concato, Peduzzi, Kamina, & Horwitz, 2001). Labrie and colleague's study was rated as "poor" by **the Annals of Internal Medicine** because of the lack of sociodemographic comparisons between groups and because death rates from other causes were not examined (Lin, Lipsitz, Miller & Janakiraman, 2008).

A separate study performed on men from Quebec sought to determine the efficacy of PSA screening by hypothesizing that changes in prostate cancer incidence from 1989 – 1993 would be attributable to the PSA test and that an inverse relationship would be observed between changes in incidence and mortality. For example, if PSA testing leads to reduced mortality, then the greater the increase in incidence due to PSA screening a greater decrease in mortality would be observed. Their variables were the magnitude of change in incidence and the magnitude of change in mortality (Perron, Moore, Bairati, Bernard & Meyer, 2002).

Perron and colleagues (2002) observed men aged 50 to 80 years by forming 15 age cohorts to adjust for age differences. They also divided the men into 15 geographical regions. Their aim was to assess the extent to which increases in incidence rates were associated with decreases in mortality rates and found no negative association between the study populations for either the age cohorts or the geographic regions noting that incidence rates increased sharply but age adjusted mortality rates only decreased slightly within the age cohorts. In other words, they did not observe that large increases in incidence were associated with large decreases in mortality with follow-up at 6 years

(Perron et al., 2002). They concluded that the magnitude in change rates between incidence and mortality was not inversely related (Pearson's r = 0.33, 1-sided p = 0.89). Similarly, by regional population, they found that a greater increase in incidence did not indicate a greater decrease in prostate cancer mortality (Pearson's r = 0.13, 1-sided p = 0.68). The authors noted limitations to their study as they only evaluated changes of incidence and mortality over one year whereas researchers suggest that magnitudes of changes should be evaluated over several years. They further reported that the Quebec cancer registry relies only on patients discharged from hospitals and increasingly, prostate cancer patients are treated as outpatient status. Finally, the authors noted that because age is a strong predictor of incidence and mortality, variations in results may have been skewed slightly because they used birth cohorts instead (Perron et al., 2002).

Well designed case-control studies can provide quality results in less time, at less cost, and do not require large numbers of subjects compared with a RCT (Otto & Roobol, 2006; Weinmann, Richert-Boe, Glass & Weiss, 2004; Concato et al., 2001). An important factor in a successful case-control study is that the control subjects must be alive at the death of their matched case subjects and without cancer at the time of diagnosis of their matched case subjects (Otto & Roobol, 2006; Weinmann et al., 2004). Case-control studies may also vary in design. However, in all studies, screening histories are determined for both the case subjects (those who have died from the disease) and the control subjects (those who have not died from the disease or those who may or may not have the disease) (Weinmann et al., 2004). It may be difficult to obtain complete and accurate screening histories especially when the screening tests can be used for

diagnosing the disease thus rendering the sample population non-representative; such may be the case in prostate screening with the PSA test. To further complicate case-control studies, African American men are considered high risk for prostate cancer, yet screening for these men is less frequent than that of Caucasian men. This can be a major drawback causing contamination bias in most research designs (Otto & Roobol, 2006; Weinmann et al., 2004).

Important disadvantages associated with case-control studies commonly include selection bias and misclassification bias (coding error). Misclassification bias occurs if a screening PSA test for a case subject is classified as a diagnostic PSA test resulting in a bias against screening. In contrast, if a diagnostic PSA test for a control is classified as a screening test, then a bias that favors screening occurs. Self-selection bias may occur when a subject presents to his physician because of "opportunistic" screening, meaning that he has a preconceived idea that he may have prostate cancer (as a result of prior testing elsewhere or symptoms) and would like to confirm the notion one way or the other and is not part of a study or population-based screening program. In addition, men at high risk (e.g., African Americans) often do not participate in community screenings due to less access to program sites or differences in their socioeconomic status (Otto & Roobol, 2006; Weinmann et al., 2004; Concato et al., 2001). In any case-control study, there should be a lower proportion or deficit of screening among cases in order to see a protective effect for the screening test. In all case-control studies the cases are matched with controls on specific independent variables and confounders (Concato et al., 2001; Concato et al., 2006).

The case-control studies evaluated by the USPSTF examined the association between the DRE and prostate cancer death, and therefore, could not make inferences regarding the PSA test. None of the three studies evaluated by the USPSTF included PSA because not enough follow-up time had elapsed from the initial dissemination of the PSA test (FDA approved in 1986) and 2002 (Harris & Lohr, 2002). However, when looking at just DRE, two of the case-control studies resulted in no association between DRE and mortality however, a third found that men who died of prostate cancer had fewer DRE exams prior to diagnosis with an odds ratio indicating only a slight protective effect for the DRE (O.R. 0.51 [95% CI, 0.31 to 0.84]). It was noted that these studies differed in methodology and design, definition of cases, reliance on individual medical records, and use of different approaches to distinguish screening DRE with clinical diagnostic DRE (Harris & Lohr, 2002).

More case-control studies emerged in the U.S. once the PSA test disseminated as a screening tool and became complimentary to the DRE. Some studies evaluated the associations of the PSA test used together with the DRE and without the DRE when examining prostate cancer deaths (Concato et al., 2000; Benson et al., 2000; Concato et al., 2001). One study used a nested case-control design to evaluate the effectiveness of either a PSA or DRE. The main hypothesis being that screening with the PSA test would be associated with improved survival and a secondary hypothesis being that using both the PSA and DRE together would be associated with further improved survival (Concato et al., 2001; Concato et al., 2006). The cohort of men came from 10 Veteran Affairs Medical Centers (VAMC) in New England during 1989 and 1990. Case subjects were

chosen from 1991 through 1995. The authors believed that a nested study design would be stronger than traditional cohort designs because only some and not all control subjects were enrolled. Case-control subjects were matched on age and on which VAMC facility they received treatment. Additionally, the authors reported a strength of the study to be that subjects were chosen from the same sample population to help reduce possibilities of unreported screening tests (Concato et al., 2001; Concato et al., 2006). For example, they had hoped to reduce bias by these two matching criteria as age is known to be associated with prior screenings and is related to mortality. And a sample of men from the same nearby 10 VA facilities would help reduce the chances of men having previous screenings outside these regions (Concato et al., 2001; Concato et al., 2006).

It was noted that because race was not specified in the VA databases it was not possible to identify subject race until the time of medical record review. The authors could not match race beforehand. Therefore, they statistically adjusted for race in the analysis portion. The authors also noted that although less than 1% of men had medical records indicating whether PSA tests were performed outside the VA system, the data was not available for non-VA screenings (Concato et al., 2006). This is a weakness of the study with possible loss of acuity for race-based disparate mortality. Further, it is believed that matching from similar facilities may weaken the study's external validity of generalizing to the population level because of the restriction to men receiving care only from within the VA system in New England.

The authors of the study cited their calculated sample size of 498 case subjects to be sufficient for a power of 80% for identifying a clinical reduction of 33% in deaths

among subjects screened with PSA (odds ratio of 0.67, alpha = 0.05, two-tailed, and beta = 0.20) (Concato et al, 2001; Concato et al., 2006). Their final cohort included 501 cases meeting inclusion criteria and thus exceeded their power calculation of 498 cases. They randomly matched 501 control subjects to each case subject on age and VA facility. Their findings of an unadjusted, matched odds ratio (OR) of 1.10 (95% CI, 0.75-1.62, p = 0.62) for PSA screening and overall mortality suggests no evidence of a screening benefit in this matched case-control sampling. After adjusting for race and comorbidity, the odds ratio for screening still remained statistically insignificant at 1.08 (95% CI, 0.71-1.64, p = 0.72) for overall mortality.

In a secondary analysis examining associations of PSA screening and cause-specific mortality, statistical insignificance was again found in an adjusted odds ratio of 1.13 (95% CI, 0.63-2.06, P = 0.68). However, when adjusting for race and comorbidity, black race presented with an adjusted OR of 4.46 (95% CI, 1.39-14.3, p = 0.01) and for comorbidity, an adjusted OR of 1.26 (95% CI; 1.01-1.57, P = 0.04) indicating a statistically significant association of PSA screening to cause-specific mortality for African Americans. The authors concluded overall that there was no evidence suggestive of a survival benefit associated with the PSA or DRE test and failed to elaborate further on the significance found for race and comorbidity.

Another case-control study was performed on members at Kaiser Permanente Northwest (KPNW) Health Plan from 1991-1999 in Portland, Oregon. Case subjects included men who were 45-84 years of age at time of death due to prostate cancer. Two control subjects were matched for each case subject on age, date of enrollment into the

plan, number of months in the health plan, and pattern of health plan membership. Controls were randomly matched to cases and had to be alive two years prior to their matched case and without prostate cancer at the time of diagnosis of their corresponding case subject. Medical chart review and death certificates were the source of data. The authors also reviewed charts and gathered data on possible covariates of height, weight, family and personal history of cancer, prior prostate related conditions and treatment (BPH, prostatitis, transurethral resection [TURP], vasectomy), tobacco use, and diabetes (Weinmann et al., 2004).

A pilot study was performed prior to the Kaiser study's initiation to determine if medical records could correctly identify PSA tests that were used for screening purposes only. PSA tests were defined as true screening tests when there were no signs or symptoms of prostate cancer noted in the medical record. As a secondary follow up to further verify medical record accuracy, telephone interviews were obtained on 97 of the randomly matched control subjects. Ninety-nine percent of the men concurred that they were without symptoms when they received their initial PSA screening tests. The final number of cases was 171 with 342 controls. The study's total population consisted of 94.7% and 95% case-controls respectively for Caucasians and only 4.7% and 1.8% case-controls for African Americans.

The results of the study indicated an inverse relation between receiving any screening test (DRE and/or PSA) and cancer-specific mortality with a reduction in mortality of 30% (OR 0.70 (95% CI: 0.46-1.1). These values show that a history of prostate screening was less common among cases than among controls thus providing a

protective effect for the controls (Weinmann et al., 2004). A major limitation to the study was that they were not able to separate the influence of a DRE on a PSA test result because the study time period included pre-PSA era (when PSA testing was not used as often) through a time in which the PSA test disseminated quickly throughout the U.S. (when PSA testing rates grew). Therefore, study subjects had more exposures to DRE than PSA screenings in the beginning of the study. They concluded that the initial rise in PSA screening during the study period may have inflated the odds ratio (Weinmann et al., 2004).

A different study, performed by many of the same authors of the previously described case-control study, sought to determine the same question of whether screening with PSA or DRE was associated with reduced prostate cancer mortality in a case-control design. However, the study used a population-based cohort of men from four health maintenance organizations (HMO). The four HMOs included the Kaiser Permanente Northern California Region, Kaiser Permanente Southern California Region, Henry Ford Health System, and Kaiser Permanente Northwest Region. Case subjects were from one of these HMOs and were either Caucasians or African Americans who died from prostate cancer between 1997 through 1999. Age groups for the men ranged from 45-84 years at time of death and men had to be members of one of the HMO plans for at least three years prior to diagnosis (Weinmann et al., 2005). Final inclusion criteria resulted in 769 confirmed cases.

Medical chart review and death certificates helped to identify case subjects who were selected if diagnosed with and dying from prostate cancer. The authors also

reviewed medical records and death certificates identifying men who were diagnosed with prostate cancer yet died of unknown other causes, who died of complications associated with prostate surgery, or who died as a result of suicide caused by complications from treatment for prostate cancer (Weinmann et al., 2005). In addition, information on other possible confounders was obtained from the subject's medical record and included height, weight, family and personal history of cancer, prior prostate or genitourinary complications or treatments (BPH, prostatitis, TURP, and vasectomy). Comorbid conditions included hypertension, diabetes and life-style habits including smoking (Weinmann et al., 2005).

Controls were randomly selected from the HMOs and were matched to case subjects on health plan, age, race, and plan membership history. One control for each of the 608 Caucasian case subjects and two controls for each of the 160 African American cases were matched. Like other case-control studies, controls had to be alive and a plan member at the time of his corresponding case diagnosis and alive at the time of his matched case's death. In addition, any control that died during the study period as a result of prostate cancer was subsequently added to the case group (Weinmann et al., 2005). Screening with PSA was defined as having at least one test during the 10 year prior to primary analysis of the patient. The authors used logistic regression, calculated odds ratios, and 95% confidence intervals for estimating the risk of mortality due to prostate cancer.

The authors categorized PSA tests or DRE according to likelihood of being performed for screening or diagnostic purposes. Categories for the study included one of

three definitions namely “definitely screening”, “probably screening”, and “no screening” (Weinmann et al., 2005). The most restricted category being “definitely screening” required that subjects have no history of prior PSA or DRE tests and that tests be performed on subjects without symptoms, no history of BPH, and no firm or enlarged prostate gland. The second category, “probably screening”, included subjects with no previous PSA or DRE test but with unchanged or improved symptoms unrelated to prostate cancer and with history of BPH or firm or enlarged glands but with no symptoms at time of tests. The third category “no screening” was defined as men who had never been screened by either the PSA or DRE (Weinmann et al., 2005).

The authors further noted that only one covariate, history of smoking, differed significantly between cases and controls (Weinmann et al., 2005). As with their first study, the ability to account for the effects of the DRE on the PSA test was impossible because most of the men received DREs. The authors noted that due to the rapid dissemination of the PSA tests during their time frame, most of the PSA tests ordered were probably meant for diagnostic purposes rather than for true screening purposes because of the number of abnormal DREs found (Weinmann et al., 2005). In addition, the authors noted that even with the rapid use of the PSA test, only 7% of the control subjects met the “definitely screening” category for PSA. Most of the tests were DRE with 74% of Caucasian cases and 83% of Caucasian controls having DREs. For African Americans, 67% of cases and 83% of the controls had DREs. The final conclusions were that having a DRE and or PSA was associated with reduced prostate mortality in Caucasians but not in African Americans. The odds ratios indicated a 30% reduction in death due to prostate

mortality for Caucasians (OR = 0.71; 95% CI = 0.53-0.94) whereas in African Americans, the odds ratio indicated no significant protective effect with screening (OR = 0.95; 95% CI = 0.61-1.5). One possible reason for the difference in odds ratio between Caucasians and African Americans included the low number of African Americans participating and thus differences could have been contributed by chance alone. Other possible reasons could have been that differences exist in patient-physician communications and that medical record notations may be different between African Americans and Caucasians. For example, if symptoms for African Americans were not recorded accurately in the medical record, then misclassification bias of diagnostic tests versus screening tests could have occurred thus falsely increasing odds ratios (Weinmann et al., 2005).

Randomized Clinical Trials

Advancements in imaging technology combined with simple non-invasive blood tests have provided physicians with diagnostic tools that have dramatically improved early detection of some cancers and proving invaluable when used for cancer screening in others (Black, 2006). However, even when using state-of-the-art technologies, there can be harms associated with screening tests. For example, false-positive results that lead to unnecessary anxiety and over diagnosis which often results in unnecessary treatment.

To help guard against the negative effects associated with inaccurate and ineffective screening tests, well designed randomized clinical trials (RCTs) may help meet this requirement. Randomized clinical trials are considered the gold standard in research design for much of medical research as well as one of the most valid study

designs for cancer screening. During the mid-1960s, the Health Insurance Plan (HIP) study proved the validity of RCTs when study results showed that screening with mammography and physical examination reduced breast cancer mortality (Black, 2006). Randomized clinical trials have also proven useful in determining the effectiveness of treatments or interventions because known (observed) and unknown (unobserved) variables are equally balanced throughout groups by randomization. The overall goal of an RCT is to simply balance the groups such that all bias is eliminated thereby ensuring that all differences in outcomes can only be attributed to differences in the treatment or intervention (Black, 2006).

There are two large randomized clinical trials that have ended, the European Randomized Screening for Prostate Cancer (ERSPC) and in the United State, the Prostate, Lung, Colorectal, and Ovary (PLCO) cancer trial. Both trials are aimed at assessing the efficacy of early screening and aggressive treatment to reduce incidence and mortality. Both trials have closed enrollment and began initial evaluation of data with hopes of determining the impact of annual prostate screening on cancer-specific mortality. A cooperative initiative between both trials was formed in 1995 so that information and datasets could be shared annually in order to combine analysis with hopes of strengthening overall results. Agreements regarding baseline measurements, procedures, collection mechanisms, and follow-up were made (Schroder, Denis & Roobol, 2003).

Key characteristics similar to both the ERSPC and the PLCO trials are age, subject exclusion criteria, and outcome. The age of men eligible for the trials is between

55-74 years. Exclusion criteria for all countries are men with preexisting prostate cancer and prior PSA tests. The outcome of interest for all countries is death from prostate cancer. Key differences in the two trials are the screening procedure and PSA threshold values indicative for biopsy. The European trial uses a cut off level of 3.0ng/ml along with a 4 year screening interval in the Spain and Sweden arm and the U.S. trial uses a 4.0ng/ml as its cut off level and an annual screening interval (Otto & DeKoning, 2004). Additional important characteristics that differ among the two trials include, type of trial, time of randomization, period of initial recruitment, identification of patient population, and source of follow-up information (DeKoning, Auvinen et al., 2002; Auviven & Hugosson, 2003).

Initial results from the ERSPC released in 2002 tested the power necessary to provide a time-frame to confirm an expected mortality reduction in prostate cancer due to screening. It was determined that a target power level of 80%-90% was sufficient but was not reached until the end of 2008 when it rose to a level of 86%. Even with sufficient power levels reached in 2008, fears of intervention effects from screened men and effects from contamination were realized in the range of 25% and 20% respectively (DeKoning, Auviven et al., 2002; DeKoning, Liem et al., 2002). The ERSPC and PLCO trials are reviewed individually with a summary listed later in the chapter.

In a randomized clinical trial performed in Sweden as a pilot study for the ERSPC, Sandblom and colleagues (2004) studied the 15 year follow-up on (n = 9,026) men aged 50-69 years with prostate cancer to test the feasibility of a large population-based screening program (Sandblom, Varenhorst, Lofman, Rosell & Carlsson, 2004).

They designed a pilot study using randomization and created a control group and a screened group of men during a three year screening interval. Data were collected on tumor stage, grade, treatment and survival for both groups with the risks of selection bias removed due to randomization. The study began in 1987 before PSA was used as a screening tool and using a 3 year screening interval to track changes over the three tests. At the first two screenings (initially in 1987 and again in 1990), the DRE was the only test used however at the third screening of 1993 the PSA was added. The study showed that 5.7% of men had prostate cancer detected in the screened group and only 3.9% in the control group. Of particular interest within the screened group, 56.5% of cancers detected were localized as T_1 or T_2 whereas within the control group, only 26.7% of men had the same disease stage ($p<0.001$). In addition, the screened group was significantly more likely to have organ-confined prostate cancer than the control group ($p<0.005$). A lower proportion of men with distant metastasis were found in the screened group and those cancers were less significantly graded than in the control group (Sandblom et al., 2004).

The authors noted that a three year screening schedule for men aged 50-69 years was sufficient for detecting early stage prostate cancer and was the first randomized clinical trial offering 15 year follow-up. They further suggested that the study would be cost-effective when considering the risk of detecting cancer early and having the disease change from a curable disease to an incurable late stage disease. Sandblom and colleagues (2004) reported that a prostate screening program was feasible when screening with both the DRE and PSA test and that these tests were effective at detecting early stage disease of prostate cancer. Disparate mortality rates among race or ethnic groups

were not investigated in the study with the population restricted to one city of 9,026 men aged 50-69 years. One limitation of the study was the small population and single geographical region of interest thus leaving power insufficient to show screening effects on mortality (Sandblom et al., 2004).

The European Randomized Screening for Prostate Cancer Trial

The ERSPC evolved out of the many discrepancies noted with use of the PSA test which, therefore, led to a need to determine whether the test may lead to reduced prostate cancer mortality when used as an early detection tool (Schroder, Denis & Roobol, 2003; Auvinen & Hugosson, 2003). Strict protocol definitions were formulated by all eight participating countries with two such definitions being the primary outcome of "prostate cancer-specific mortality" and "not all cause mortality". This was decided mainly because subjects within RCTs are free of the disease and only cancer-specific mortality is influenced by screening for the disease (DeKoning, Hakulinen et al., 2003). Therefore, the definition agreed upon for subjects to meet the endpoint of cancer-specific mortality include those men having died, known to have prostate cancer, and where prostate cancer was listed on the death certificates.

The ERSPC has recruited approximately 193,000 men since 1992 from eight European countries. There are differences within study parameters for the European trial due to multiple centers being involved. Some differences include age variations (from 50-74 years old), PSA threshold values, and screening intervals (DeKoning, Auvinen et al., 2002). For example, PSA thresholds were set to $\geq$ 4.0ng/ml in all countries except Spain

and Sweden, where thresholds of ≥ 3.0ng/ml and ≥ 4.1ng/ml were used respectively. The ERSPC has maintained a 4 year interval for screening.

Noted limitations of the European trial include selection bias and contamination by opportunistic screening of the control arm. For instance, it is possible for subjects who choose to participate do so because they are symptomatic or know they may be at increased risk for prostate cancer and simply wish to rule it out. It is also possible that men who participate are healthier and care more about their health. These forms of selection biases were not controlled for in the ERSPC because the authors noted that it was impossible to measure their extent and effect on power (DeKoning, Liem et al., 2002; Schroder et al., 2003).

Contamination bias by opportunistic screening could also affect power. In an ideal study, men in the control group would not have been screened prior or during the study; however, that proportion of men in a control group who have received screening prior to trial dates is called the contamination rate. Opportunistic screening occurs when men within a control group received PSA testing at any time prior to trial enrollment either by their own submission or by a physician's suggestion in a prior clinical visit (Ciatto, Zappa et al., 2003).

A study to determine contamination rates and its effect on power evolved from the Rotterdam section of the ERSPC data in 2003. The study noted that PSA contamination (testing of asymptomatic men in the control group) could adversely affect the power of the ERSPC trial (Otto, Van Der Cruijsen et al., 2003). The authors eventually reported only an 8% contamination rate with less than half of those men being

diagnosed with prostate cancer. The authors concluded that PSA contamination in the trial should therefore, not lead to power problems as initially thought (Otto, Van Der Cruijsen et al., 2003).

Additional pilot studies from the Rotterdam and Netherlands section of the ERSPC trial were performed to assess the randomization and testing procedures to, hopefully, show that continuing the ERSPC trial was warranted (Schroder, Denis & Roobol, 2003; Schroder, Roobol et al., 2005). The numbers of deaths for any cause were not significantly different at 19.2% and 20.9% respectively. Furthermore, 20% of the screened group and 32% of the control group died with prostate cancer, whereas only 2.7% of the screening group and 17% of the control group died from prostate cancer. The authors noted that none of the pilot studies could provide any statistical analysis because of the lack of power, yet still believed continuing the trial seemed reasonable (Schroder, Roobol et al., 2005).

Other studies have emerged that evaluated overdiagnosis and over treatment from the ERSPC trial data. Among those was one study in the Rotterdam section of the ERSPC that enrolled 42,376 men and reported 1,498 cases of prostate cancer during 2003 (Draisma et al., 2003). They reported that lead times and overdetection could result in unnecessary treatment. Lead time is the time in which diagnosis of prostate cancer is increased by screening. Specifically it is defined as the amount of time between prostate cancer detection and either clinical diagnosis without screening or death of other causes. Overdetection occurs when cancers are found that would have never been detected in a man's lifetime in the absence of screening. Both of these consequences have a large

impact on the net benefits of screening. Draisma and colleagues (2003) found that a man's age was significant to predicting these rates noting that a mean age of 55 resulted in a lead time of 12.3 years and the overdetection rate was 27%. This means that a man age 55 would probably have been asymptomatic and not clinically diagnosed with prostate cancer until age 67.2 years and that 27% of those men diagnosed would have most likely received unnecessary treatment because of the early detection. At age 75, these rates changed to 6 years and 56% respectively. Draisma and colleagues (2003) further noted that their screening program increased the lifetime risk of prostate cancer diagnosis from 6.4% to 10.6% a relative increase of 65%. These results suggest that regular screening for prostate cancer may advance a diagnosis by 10 years with about half screen detected men not having been diagnosed without screening. The authors concluded that screening rates of greater than one year should be applied to Dutch men of the Netherlands and that screening for prostate cancer is likely to be associated with early diagnosis with considerable overdetection. The study did not look at different races or ethnic groups within the Rotterdam registries considering only men of Dutch origin (Draisma et al., 2003).

Similar studies examined the effects of over diagnosis due to screening. These studies included reviewing the magnitude of overdiagnosis and its impact on unnecessary treatment in men who may otherwise have insignificant indolent tumors (Etzioni, Penson, et al., 2002; Ciatto, Gervasi et al., 2004; Graif et al., 2007). Etzioni and colleagues (2002) developed a computer model to test relationships of the PSA test, diagnosis of prostate cancer, and death based on assumptions from the ERSPC trial. They found that after

hypothetically testing two million men age 60-84 years and using known parameter estimates for the expected lead times and incidence rates, the computer model predicted similar results observed by SEER registries during the decade 1988 through 1998; those being 29% in Caucasians and 44% in African Americans.

Ciatto's group (2004) agreed that overdiagnosis depends on age and the magnitude of the lead time associated with detection through screening (Ciatto, Gervasi et al., 2004). Their study indicated that overdiagnosis is prevalent in the ERSPC trial (Ciatto, Gervasi et al., 2004).

In a separate study examining the frequency of over and under diagnosis from two large cohort groups of men receiving prostate surgery, Graif and colleagues (2007) found that 27% of the 2,126 men reviewed were under diagnosed and only 5% were over diagnosed (Graif et al., 2007). These authors argued that although over diagnosis is existent, under diagnosis is also occurring and attention should be given to the cancers being missed without screening. Interestingly, a secondary finding from the study showed that decreasing the PSA threshold from 4.0 ng/ml to 2.5 ng/ml resulted in a reduction in the under diagnosis rate and an increase in the 5 year survival rate. The authors concluded that perhaps lowering the PSA threshold level from 4.0 ng/ml to 2.5 ng/ml should be considered when examining optimal screening protocols.

Two additional studies have emerged out of the Rotterdam section of the ERSPC which examined the progression of PSA over time (Schroder, Raaijmakers et al., 2005; Gosselaar et al., 2006). One study examined the time it took for PSA values to increase to 3.0 ng/ml after a four year follow-up in men presenting with PSA values < 3.0 ng/ml at

the first round of screening (Schroder, Raaijmakers et al., 2005). The study consisted of 6,467 men randomized within the ERSPC and eligible for a second round screening at the 4 year interval. The results show that men who presented at the first round with PSA values ranging from 3-3.9 ng/ml showed an increase in the proportion of cancers found in the second round. However, men who presented with PSA values ranging from 4-9.9 ng/ml in the first screening remained unchanged at the second screening. Finally, men who presented with PSA values of > 10.0 ng/ml at first screening round showed a decrease in detecting cancers in the second round. An additional finding of the study confirmed other reports that PSA progression rates for men presenting with initial first round screenings of < 2.9 ng/ml was low suggesting that longer screening intervals may be appropriate for these men. The study concluded that since most of the cancers detected in the second round of screening occurred in men with PSA values of 3-3.9 ng/ml, a cutoff threshold of 3.0 ng/ml is a valid suggestion for second round screenings and longer screening intervals (Schroder, Raaijmakers et al., 2005). These data further support the change from 4.0 ng/ml to 3.0 ng/ml in the ERSPC trial; however, in the U.S. screening intervals remain at annual rates and 4.0ng/ml continues to be the threshold value.

The second study also examined the 4 year progression of PSA test values at the second screening round with the hopes of reducing unnecessary biopsies by possibly increasing screening interval times and thus saving the health care system money (Gosselaar et al., 2006). The authors concluded that omitting the DRE and TRUS did not change the amount of interval cancers or detection of prostate cancers after 4 years and the decision to omit these tests from the ERSPC seemed justified (Gosselaar et al., 2006).

Therefore, it is logical to believe that if asymptomatic men who participate in population-based screenings have low initial PSA values that remain relatively unchanged over time, the likelihood of them progressing to values >4.0 ng/ml is minimal which is supportive of longer screening intervals and saving the health care industry millions of dollars in overdiagnosis and over treatment (Schroder, Raaijmakers et al., 2005). Further, if these groups of men omitted the DRE/TRUS tests at second round screenings, even more savings could be realized by reducing the numbers of unnecessary and costly biopsies (Gosselaar et al., 2006).

Another study of men from the Rotterdam section of the ERSPC examined prognostic factors associated with the screened group and control group (Van Der Cruijsen-Koeter et al., 2005). Authors evaluated over 35, 000 men aged 55-74 years randomized during 1993-1999. The final selection included 17,635 men in the screening group and 17, 513 men in the control group. The goal was to determine screening characteristics between the two groups over a series of screening rounds. The prognostic factors evaluated were TNM staging and Gleason Score grading. Results showed both a favorable shift in stage and Gleason score in the screening group. For example, 84.2% of the cancers were detected in the screening group and 58.9% in the control group with most tumors being staged at $T_1$and T_2 (Van Der Cruijsen-Koeter et al., 2005). An important finding was differences in the numbers of men found to have distant metastasis in that within the screening group, only 7 men had advanced metastatic disease and within the control group, 27 men were found to have distant metastasis. Moreover, out of the total number of men, there was a 5.0 times greater likelihood of finding distant

metastasis in the control group which was statistically significant to the screening group at a $p < 0.001$ (Van Der Cruijsen-Koeter et al., 2005).

Limitations to the study were noted with contamination rates of approximately 5% from opportunistic PSA screening of the control group. The authors noted this rate to be comparable to a study by Otto and colleagues (2003) who also used the Rotterdam section of men where percentages of PSA contamination rates of 7.6% and 3.3% were found in the control group and screening group respectively (Van Der Cruijsen-Koeter et al., 2005).

A different study of the Rotterdam section examined PSA changes in men with and without prostate cancer after a four year period between two screening rounds. The authors acknowledged use of the PSA test as not being a proven cancer detection tool that also reduces cancer-specific mortality. Therefore, they focused on changes over time of the sub-forms of PSA such as the PSA velocity (PSAV), the PSA slope, and the PSA doubling time (PSADT) in men with positive, negative, and no biopsy indicated over a four year period after the initial first round screening. The PSA velocity was defined as how fast a PSA value rises from its initial value over one year. In the U.S. a PSA rise of 0.75 ng/ml/year usually implies additional clinical work up be initiated. The PSA slope was defined by taking the differences between the base 2-logarithms from the initial PSA value and the second round PSA value and dividing by the time interval between the measurements. The PSA doubling time (PSADT) is the time it takes for an initial screening PSA result to double in value. The greater the velocity or doubling time of a PSA indicated a faster progression of disease to a more aggressive stage (Raaijmakers et

al., 2004). The results indicated that men with prostate cancer had a mean PSAV of 0.62 ng/ml/year compared to men with no prostate cancer having a mean PSAV of 0.46 ng/ml/year ($p = 0.001$). The PSADT was 5.1 years and 6.1 years in men with and without prostate cancer respectively ($p = 0.002$). The authors tried to improve specificity (reducing numbers of unnecessary biopsies) by fixing the sensitivity at 95% (which means that 95% of cancers would accurately be predicted). This review resulted in a PSAV specificity of 12.5% which indicates that 12.5% of the biopsies would be unnecessary while still accurately detecting 95% of the cancers. The PSADT resulted in saving 13% of unnecessary biopsies. The authors confirmed other reported observations of the lack of the specificity in the PSA test as the only indicator for biopsy. For example, it has already been observed that in only about 20-30% of men receiving biopsies and having PSA values > 4.0 ng/ml, that prostate cancer is detected. This leaves 70-80% of men having false positive test results leading to overdiagnosis and over treatment of possibly indolent cancers. The authors concluded that the sub-forms evaluated in their study could be helpful in improving screening guidelines. The authors noted limitations as only having two PSA test results over time and conceded that more tests over longer periods would be necessary to strengthen internal validity for use of the sub-forms of PSA (Raaijmakers, 2004). Additional limitations included using only the relative sensitivity of the sub-forms of PSA, in that using biopsy results for prostate cancer detection as the reference standard does not provide the absolute sensitivity and therefore, does not allow an understanding of the true numbers of cases that go undetected (Raaijmakers, 2004).

A similar study from the Switzerland arm of the ERSPC examined 7,124 men of whom 3,562 were randomized to the screened group and 3,562 men to the control group. Kwiatowski and colleagues (2004) found a prostate cancer detection rate of 2.5% in PSA tested men and only 7% of the men had distant metastasis while 93% had organ-confined disease. The authors concluded that the results suggested not recommending large screening programs and instead, physicians should have informed discussions with their patients at consultation concerning the risks and benefits of screening (Kwiatowski et al., 2004).

An additional study coming out of the Swedish section of the ERSPC examined the efficacy of PSA screening after a two year screening interval over an eight year period (resulting in 4 PSA measurements). Out of the 32,298 men enrolled as part of the Swedish arm, 10,000 men each were randomized to either the control group or screening group. Men with PSA values < 3.0 ng/ml received no further testing and were invited to return after two years, four years, and then six years for repeat evaluation. Men with PSA results > 3.0 ng/ml were offered further workup by a urologist for consideration of a DRE, TRUS, and sextant biopsy (Hugosson, Aus, Lilja, Lodding & Pihl, 2004; Schroder, Habbema, Roobol & Bangma, 2006). The authors noted that PSA was highly associated with prostate cancer risk in the first screening round with 14% of men with PSA levels between 3.0 and 4.0 ng/ml being diagnosed with cancer. However, the risk decreased significantly in the third and fourth rounds of screening (Hugosson et al., 2004). The results noted that stage shifts corresponded with PSA levels to where advanced and metastatic diseases were relatively nonexistent in the later screening rounds when PSA

levels tended to be lower. The authors noted that these findings were consistent with Labrie's study (2004) of the Quebec randomized trial. The study reported a 73% participation rate with results showing that during the eight year screening period only 43 interval cancers were detected compared with 550 cancers found in the screened group and 197 cancers found in the control group. The authors concluded that the study showed that a two year screening interval was sufficient for detecting most cancers in the first round and that PSA screening does likely lead to stage and grade shifts with most tumors being detected at curable stages (Hugosson et al., 2004; Schroder, Habbema et al., 2006).

The most recent study from the ERSPC published in the "New England Journal of Medicine" in March of 2009 identified 182, 000 men randomly assigned to either a treatment group receiving a PSA test every four years or a control group that did not receive any PSA testing (Schroder et al., 2009). The outcome of interest was prostate cancer specific mortality. It was determined that 82% of men from the screening group had at least one screening test offered. After a median 9 year follow up period, the incidence rate was 8.2% in the treatment group and 4.8% in the control group. The death rate ratio in the screened group compared with the control group was 0.80 (CI, 0.65-0.98; adjusted p value = 0.04) and the absolute risk difference was 0.71 death per 1000 men. This means that 1,410 men would have to be screened with 48 new additional cases of prostate cancer being treated in order to prevent one death from prostate cancer (Schroder et al., 2009). The authors concluded that screening PSA reduced the risk of dying from prostate cancer by 20% but was also associated with a high overdiagnosis risk (Schroder et al., 2009).

The ERSPC is not without limitations as initial findings from the Rotterdam section have illustrated. Biases of lead time, length, and selection may diminish the importance of such findings. For example, when comparing 1,014 men with screen detected prostate cancer within the screening group of the Rotterdam section with a control group from the same region, results indicate that after a 5-year follow-up period, only 2% had died from prostate cancer (Albers, 2007). The authors of those studies concluded that men of the screening group had a 98% survival rate and that these men were less likely to die before the 5 year follow-up period. However, this should not be surprising because men of screened groups are usually seen by their physician more often and that screen detected cancers usually are of early stage and localized, therefore, the higher survival rates experienced by these men may be attributable to lead-time bias. Even more disappointing is the conclusion that because initial results showed low numbers of deaths from prostate cancer, final conclusions from the ERSPC may not be drawn for more than the original 10 years thought to be sufficient and therefore continued follow-up periods may need to be extended out to 15 years ending in 2013 (Albers, 2007; http://www.cancer.gov/newscenter/qa/2009/plcoprostateresultsqa assessed February 2011). Another possible disappointment of the ERSPC is the overdiagnosis and over treatment during the trial period. For example, there are a high percentage of patients who received surgery that may have been candidates for active surveillance instead. This is because at the time, it was not known that active surveillance was an important treatment option for these men. Because of this important finding, almost thirty three percent of men in the ERSPC would have been active surveillance candidates; however, 90% of

them chose aggressive treatment with increased side effects. Therefore, this change in treatment during the trial period may also bias the results.

Finally, should long-term follow-up results show screening to be valuable at reducing cancer-specific mortality, it could be argued that active surveillance should have been offered more. In contrast, should final results show screening to be a poor predictor of reducing cancer-specific mortality, it could be argued that opportunistic screening rates were too high in the control group (Albers, 2007). What may prove to be important factors provided by the trial are changes in treatment management of prostate cancer, baseline PSA values, frequency of PSA testing, and threshold values of PSA for different age groups (Albers, 2007). Race was not adequately represented in the ERSPC trial or adequately understood in studies involving large population-based areas when evaluating disparate mortality rates.

The most current result, as described earlier, is that nine year follow-up indicated a 20% reduction in cancer-specific mortality among the screened group compared with the non-screened group in men aged 55-69 years thus implying a survival benefit to PSA screening. The trial also resulted in a 40% increase in the number of prostate cancers diagnosed in the screened group during the same follow-up period (http://www.cancer.gov/newscenter/qa/2009/plcoprostateresultsqa assessed February 2011).

The Prostate Lung Colon and Ovarian Trial

The PLCO cancer screening trial began recruitment in 1993 and closed in 2001 with 154,942 total subjects enrolled including men and women from 10 cancer centers

across the U.S. The participating centers include the University of Colorado Health Sciences Center, the Lombardi Cancer Research Center of Georgetown University, the Pacific Health Research Institute, the Henry Ford Health System, the University of Minnesota School of Public Health/Virginia L. Piper Cancer Institute, the Washington University School of Medicine, the University of Pittsburgh/Pittsburgh Cancer Institute/Magee-Women's Hospital, the University of Utah School of Medicine, the Marshfield (Wisconsin) Medical Research and Education Foundation, and the University of Alabama at Birmingham (Roemeling, 2006; Andriole, Levin et al., 2005).

Subjects completed questionnaires on many baseline factors such as diet, tobacco and alcohol use, family history of cancer, use of certain selective drugs, and other risk factors. Recruitment was accomplished mainly through mailings (Pinsky, Ford et al., 2008). All blood samples collected for PSA testing were stored in a central repository to allow for multiple study reviews (Andriole, Reding, Hayes, Prorok, & Gohagan, 2004).

Men in the screened group were randomized, they received both a DRE and PSA test, they were of the ages 55-74 years old, and had no previously reported cases of cancer. These men received subsequent screening tests 12 months later each year for a total of six years of screening. Exclusion criteria included current treatment for cancer (except skin cancers), surgical removal of the entire prostate gland, participation in a different cancer-screening or primary prevention trial, and use of finasteride in the past six months. Finasteride (Proscar) is used to treat BPH and male balding and is one of two 5-alpha-reductase inhibitors used to treat BPH, the second drug is known as dutasteride (Avodart). Both these drugs are equally effective for treating BPH and can reduce the

size of the gland by 20-30%. Finasteride is also known to reduce PSA values by as much as 50% and therefore could bias the PSA results for the trial (Carter, 2007; Andriole, Reding et al., 2004; Ford, Havstad, Demers & Johnson, 2005).

Baseline socioeconomic demographics were gathered using a self-reporting questionnaire. Baseline PSA tests were performed using the Hybritech Immunoassay method (Beckham-Coulter, San Francisco, CA) with values > 4.0 ng/ml as the threshold value indicating possible cancer. Men with suspicious DRE or PSA were referred to their physician for additional work up.

Because the National Cancer Institute and the Centers for Disease Control wanted to maintain ethnic diversity throughout the PLCO trial, they funded several activities to ensure that African Americans were adequately represented in the trial. Adequate representation would also assure distribution of appropriate information of the risks and benefits that would increase understanding of the possible interactions of treatment effects based on biological, social, and cultural factors associated with race (Pinsky, Ford et al., 2008; Stallings et al., 2000).

The factors included in the decision making process for African American men to participate consists of cultural differences, perceptions of health care, and disparities in access to good quality care. Therefore one goal of the PLCO was to answer questions as to whether the current PSA threshold of 4.0 ng/ml should be different based on race and should African American men begin screening for prostate cancer at the same age as Caucasian men. These are questions that can only be answered if different ethnic groups are well represented. Unfortunately, as the trial recruitment ended, minority enrollment

made up only 14%, of which 6% were non-Hispanic blacks (Stallings et al., 2000). In order to address this low minority rate, the NCI and the CDC formed new projects during 1997 aimed at understanding and overcoming barriers of participation in the trial and to increase the minority enrollment by 32%. For example, the African American Men Project (AA men at Henry Ford Health System in Michigan) was created and is a randomized trial designed to evaluate the efficacy of new ways to increase recruitment of African American men. In addition, a minority-based screening center was started at the University of Alabama, Birmingham to identify factors that influence the decisions of African American women who participate in the PLCO trial, and two behavioral research projects at the University of Pittsburgh were designed to evaluate the psychological factors that influence African American decisions to participate in cancer screening research (Stallings et al., 2000; Pinsky, Ford et al., 2008). The attempts made by the PLCO to have minority groups better represented were not as successful as originally planned but were similar to other multicenter cancer screening trials like the Prostate Cancer Prevention Trial, the STAR trial, the CARET trial, and the SELECT trial (Pinsky, Ford et al., 2008). The final results of the PLCO are a few years away; however the initial screening round is complete and is made up of 38,355 men in control group and 38,350 men in the screened group of the prostate arm of the trial. Clinical staging was assigned based on tumor extent using the TNM system and the AJCC method previously described. As discussed above, minority representation was less than had hoped as African American men represented only 4.5% of the screened group; whereas, 86.2% of men in the screened group were Caucasian. All age groups were well represented with

about half having college degrees. Compliance rates were similar across all age groups. Among men with abnormal DRE, PSA values less than 4.0ng/ml, and a biopsy, cancer detection rates were calculated as 3.2%, whereas men with positive DRE and PSA levels greater than 10.0 ng/ml, a 76% overall prostate cancer detection rate was calculated (Andriole, Levin et al., 2005). When considering the PSA test alone (without DRE) in men having PSA values > 4.0 ng/ml and who had a biopsy, a cancer detection rate of 18% was found. The overall cancer detection rate on all 34,244 men having an initial PSA or DRE was only 1.6%. This rate varied with age from 1.0% for men 55-59 years to 2.5% for men 70-74 years (Andriole, Levin et al., 2005).

In summary, the PLCO trial has not yet reported 10 year data but only initial results from baseline first round screenings. After six rounds of annual screenings (7 years), cancer detection rates increased by 22 % in men of the screening group with 50 deaths and 44 deaths in the non-screening group. The difference in these numbers was not statistically significant and therefore, no survival benefit could be associated between PSA screening and mortality. These rates differ from the Rotterdam section of the ERSPC trial in that first round screenings from the ERPSC found a prostate cancer detection rate of 4.2%. The authors explained the difference as possibly being due to the higher biopsy rates in the ERSPC versus the PLCO (91% in the ERSPC and 31.5% in the PLCO). The ERSPC trial protocol called for specific follow-up in men with positive screening findings, whereas in the PLCO trial, men were referred to their primary health care provider for discussion of further work-up. Trial protocols may reflect differences in the U.S. and Europeans practice patterns within the medical community (see Table 5).

Table 5. Characteristics of Initial Findings from the PLCO Trial.

Control group	Screened group	Proportion Caucasian AA
n = 38,355	n = 38,350	86.2% 4.6%
Number of men having both a PSA & DRE (n = 34,244) [45%]		
Of which had positive results on both tests	Positive results on one test	Negative results on both tests
1.2%	12.9%	85.9%
Cancer Detection Rate		
Among all men with +DRE and PSA < 4.0		3.2%
Among all men with +DRE and PSA >10.0		76%
Among all men having PSA alone and biopsy With initial PSA > 4.0		18%
Variation with age group 55-59 yrs. 70-74 yrs.		 1.0% 2.5%
Overall for all men having either DRE or PSA		1.6%

In a separate study using data of the PLCO trial from the Henry Ford Health System, authors evaluated what effects false-positive results had on men returning for additional screenings. Out of the total 4,093 men from the health system, 2,290 qualified to participate. The demographic characteristics showed that 85.9% of the men were Caucasian and 14.1% were African American with all other ethnic groups excluded due to low numbers. The average age was 62.8 years and 71.6% had greater than a high school education. A univariate analysis for categorical covariates and screening behavior showed a strong association that men receiving a false-positive base line result from screening would most likely not return for his 12 month second round screening. Specifically, an odds ratio of 1.96 (95%CI, 1.36-2.83, $P < 0.001$) suggests that men were almost twice as likely not to return for subsequent screening when receiving a base line

false-positive result compared to men receiving a base line negative result (Ford, Havstad, Demers & Johnson, 2005). African American men were also less likely to return for a 12 month second round screening with an odds ratio of nearly 1.8 (95% CI, 1.2-2.6, $p = 0.002$). Finally, education level showed a significant negative association (OR 1.71; 95%CI, 1.25-2.34, $p < 0.001$) and age was not statistically different with and odds ratio of 1.02 (95%CI, 0.99-1.05, $p = 0.10$). The authors noted one strength of the study as adequate representation of African American men (14%). A limitation of the study included that any information gained from subjects who agreed to participate in a long-term screening trial may not be representative of the population because these individuals may be healthier. Furthermore, the authors noted that the results may not be generalized across other geographic regions. The final conclusions indicated a more shared decision making process between patient and provider discussing the meanings of false-positive results and their implications (Ford, Havstad, Demers et al., 2005).

Another study to evaluate the probable time for low PSA levels (normal levels) to increase to higher levels (abnormal values) was examined using the PLCO data. A large proportion of screened men have PSA values less than 4.0 ng/ml which raises the question of when this group of men should return for subsequent screening intervals (Crawford et al., 2006). The study showed that the estimated probability for men with normal PSA values to convert to abnormal values varied with time. The results from this study suggest that a reduction in PSA tests, and therefore costs, could have been realized (Crawford et al., 2006). These results were similar to those found in the initial screening rounds from the ERSPC trial. Since a large proportion of men being screened had base

line PSA values of less than 2.0 ng/ml, reducing the number of PSA tests could result in a cost reduction as well (Crawford et al., 2006).

In a separate study, researchers examined the "healthy volunteer effect" of the PLCO trial. Volunteers of screening trials tend to be healthier and more educated due to specific criteria of the study protocol (Pinsky, Miller et al., 2007). Certain inclusion and exclusion criteria can target healthier individuals who tend to be more educated, have higher incomes and lead healthier lifestyles. The study examined this health effect for cause-specific mortality rates. Unfortunately, the study excluded cancers as one of the incidence and mortality ratio computations and African American men only represented 4.4% of the population within the study (Pinsky, Miller et al., 2007). In addition, study findings showed that being African American, ever have smoked, low education, lack of physical activity, and not married were all associated with increased mortality (Pinsky, Miller et al., 2007).

A more recent study emerged from within the PLCO that evaluated effects of baseline comorbidities on adherence to clinical trial protocols. In addition, factors such as age, race, gender, and psychological behavior that could affect whether subjects participating in clinical trials adhere to protocols were examined. African American men typically have low participation rates in cancer screening trials although they have higher incidence and mortality rates. The study sample was composed of 683 African American men older than 55 years from the Henry Ford Health System within context of the PLCO trial. The men were assigned either to a case management screened group (n = 344) or to a case management control group (n = 339). The case control managers received the

screening results and the baseline health histories of comorbidities. Health histories were obtained from the self-reported questionnaires (Ford, Havstad, Fields et al., 2008). The study hypothesis was that participants with comorbidities would show lower adherence rates to PLCO screening than participants without any comorbidity (Ford, Havstad, Fields et al., 2008). The results indicated no significant differences found between any of the health history conditions listed. The only comorbid condition showing a negative statistical significance (less likely to adhere to protocol) on adherence to the PSA test was smoking with an odds ratio of 0.6 (95% CI; 0.4-0.9, $p < 0.05$) for the PSA test. Family history of cancer showed a positive association to the DRE test (more likely to adhere) with an odds ratio of 1.5 (95% CI; 1.0-2.2, $p < 0.05$). The authors were also interested in whether the number of comorbid conditions would show an interaction to adherence, however the results indicated neither a positive or negative trend in adherence could be associated with the number of comorbidities ($p > 0.30$). The authors concluded that African American men with comorbidities were as likely to participate in clinical trials as Caucasians. The authors suggested limitations to include African American men from the Detroit metropolitan area and the baseline questionnaire did not include psychiatric comorbidities. Strengths of the study were that focus was on older African American men who tend to have higher incidence and mortality rates of prostate cancer. In addition, the study population was from a large metropolitan area that tended to be socio-demographically representative of other larger urban areas so it is likely that these results may be generalized to older African American men from those regions (Ford, Havstad, Fields et al., 2008).

The most recent and first report coming out of the PLCO trial was published in the New England Journal of Medicine in March 2009. The aim was to note screening effects with PSA and DRE on prostate cancer-specific mortality (Andriole et al., 2009). The authors randomly assigned 76,693 men from 10 U.S. centers to receive either annual PSA screening or usual care, defined as sometimes including screening. The screening group received annual PSA tests for six years and a DRE for four years. The screening group compliance rates consisted of 85% for PSA testing and 86% for DRE testing with rates increasing from 40% in the first year to 52% by the sixth year for PSA testing (Andriole et al., 2009). Results after 7 years of follow up indicated the incidence of prostate cancer to be 116 cases (2,820 cases) per 10,000 person-years in the screening group and 95 cases (2,322) per 10, 000 person-years in the control group. These results show a rate ratio of 1.22 (CI, 1.16 to 1.29). The incidence of death per 10,000 person-years was 2.0 (50 deaths) in the screening group and 1.77 (44 deaths) in the control group (rate ratio, 1.13, CI, 0.75 to 1.70). The authors concluded that after the 7 year follow up period, the mortality rate from prostate cancer was low and did not significantly differ between the two groups (Andriole et al., 2009).

It is recognized that performing a study showing that screening can effectively reduce death rates and improve quality of life requires large resources. The PLCO study of the National Cancer Institute was based on the assumption that 74,000 men and a 10 year follow-up period would be required to achieve sufficient power and to show that screening directly leads to reduced mortality due to slow growth progression rates of prostate cancer (Sandblom, 2004). With final results not available until further follow-up

reported, concerns for high risk contamination rates to the control groups because of previous screenings and the late start of the trial loom (Labrie et al., 2004).

SEER-Medicare Screening Studies

In addition to the population-based randomized trials from other countries and the PLCO listed above, there have been numerous smaller studies in the United States using some of the same variables as the larger studies, however, most included race as an independent variable as well. In looking at a comparison of PSA use among African American and Caucasian men from 1991-1998, Etzioni and colleagues (2002) reported that among Medicare claims data of elderly men PSA use had reached nearly 35% for Caucasians and 25% for African Americans during 1996. The authors concluded that older African American men were less likely to receive a PSA test than older Caucasian men and that regular screening in African Americans was lower than in Caucasians (Etzioni, Berry et al., 2002). Their study used SEER registry data from 13 geographic regions covering 14% of the U.S. population showing consistency between other survey data of screening behaviors between African Americans and Caucasians. Namely, that African Americans were less likely to use PSA screening; however, the actual testing rates estimated from the SEER registries indicate that the discrepancies may be lower than expected. Etzioni and colleagues (2002) determined that by 1998, approximately 38% Caucasians and 31% African Americans received a PSA test at least annually. This translates into an odds ratio of 73%, a much greater ratio than reported from the New York Behavioral Risk Surveillance System (BRFSS) that estimated a ratio of 30% (Etzioni, Berry et al., 2002). Etzioni and colleagues (2002) concluded that this difference

may be due to the use of SEER registry which is an administrative claims database with results indicative of multiple areas combined unlike single area survey data.

One substantial limitation when using SEER-Medicare linked datasets is the fact that the amount of heterogeneity across regions is extremely great. This was illustrated by Legler and colleagues (1998) earlier where they noted an association between prostate incidence and first-time PSA use in two SEER areas having different PSA testing patterns (Legler, Feuer, & Potosky, 1998). Etzioni and colleagues (2002) also found large differences in testing patterns across SEER areas where Caucasians, surprisingly, had higher PSA testing rates in areas of greater African American populations such as Atlanta, Detroit, and Los Angeles. Caucasians had the lowest testing rates in Connecticut, Utah, and Iowa where their population was greater.

Many variables are thought to be associated with the complex interrelations surrounding differences in prostate screening and mortality rates among races, especially in the U.S. and among African American and Caucasian men. Furthermore, use of a recent large administrative claims database coupled with the robust statistical method of propensity score analysis for mimicking randomization in this thesis will encourage exploration into the complexities of racial differences that will benefit educational programs, other research quests, and public policy. These ideas are supported in a study describing use of the SEER-Medicare data. The SEER-Medicare data provides for large population-based cohort studies that can be used longitudinally for tracking cancer, diagnosis, treatment, and outcomes (Warren, Klabunde, Schrag, Bach & Riley, 2002). However, one challenge of using observational data such as the SEER-Medicare files is

that participants are not randomly assigned and in order to make meaningful inferences researchers must control for differences in groups. Methods such as propensity scoring are recognized as analogous to randomization and therefore, the combination of the most recent SEER-Medicare dataset and a propensity analysis will be useful for describing disparate mortality rates and prostate screening in this study.

Risk Factors and Prostate Cancer

A summary of the studies associated with risk and prostate cancer are provided later in the chapter. An EPA report from 2004 placed risk factors associated with prostate cancer into two groups, endogenous and exogenous. Endogenous risk factors include family history of disease, hormones, African American race, and aging. Exogenous risk factors included diet (weight and obesity), environmental agents, occupation, and physical activities. Current knowledge of causes and prevention for prostate cancer remain unclear and virtually nonexistent (Bostwick et al., 2004).

Among endogenous risk factors, family history is important. Men are two to three times more likely to develop prostate cancer if they have first degree relatives with prostate cancer (i.e. father, brother, son). However, the EPA report suggests that this association may be contaminated by selection bias as the clinical and pathological features of familial cancer can be similar to nonfamilial cancer (Bostwick et al., 2004; U.S. Preventive Services Task Force, 2002). Other studies have found that family history is consistently positively associated with prostate cancer risk and appears to have a stronger association than colon or breast cancer. For example, one epidemiological study found that African American men with known family history had a higher risk for

prostate cancer (odds ratio [OR] 3.2) compared with Caucasian men (OR 1.9), although the numbers were not significantly different (Whittemore, Wu et al., 1995). An additional study showed that 31.2 % of African American men reported a family history compared to only 22.2% of Caucasian men (Cotter, Gern, Ho, Chang & Burk, 2002).

It is suggested that male hormones such as androgen and testosterone can affect cancer growth rates and tumor progression by actually changing clinically indolent tumors into more clinically apparent and aggressive tumors. Findings have shown that high levels of testosterone might increase a man's risk over time although these studies also noted results that were inconsistent in confirming this relationship (Bostwick, 2004; Prostate Cancer Initiative-Centers for Disease Control and Prevention [CDC], 2007) (see Table 6). It has been hypothesized that testosterone may play an important role in developing prostate cancerous cells that could function as tumor catalysts. Testosterone promotes cell division that may result in an accumulation of spontaneous mutations over a lifetime and then suddenly appear in normal prostate tissue. Whatever its role, testosterone is most likely only a cofactor for prostatic carcinogenesis (Bostwick, 2004).

Prostate cancer risk by race continues to be an important topic as African American men have the highest incidence of prostate cancer in the world. The risk for an African American man is higher than for Caucasians, Asians, Hispanics, Pacific Islanders, and Native Americans. From 1988 to 1992, race-specific incidence rates in the United States ranged from the lowest of 24.2 per 100,000 for Koreans to the highest of 180.6 per 100,000 for African Americans (Bostwick, 2004). African Americans are more likely to present with advanced stage and their stage-specific mortality is worse than in

Table 6. Summary of Screening Studies, RCTs, and Case-Control Studies.

Author (year)	Study Category	Study type or dataset	Outcome measure	Finding (s)	Limitations
Crawford (2008)	Screening by PCPT	Literature review	Value of PSA	As PSA rises Sensitivity decreases and Specificity increases	None mentioned
Harris & Lohr (2002)	Screening by USPSTF	RCT	Efficacy of screening on mortality	No difference in mortality between groups (8yr follow-up)	Low participation
Labrie et al. (2004)	Screening	RCT extension to above study	Efficacy of screening on mortality	62% reduction in mortality between groups (11yr follow-up) Age significant	Low response rate (23.6%) Ethnic groups not evaluated Susceptibility bias high Lack of sociodemographic comparisons Death rates from other causes not evaluated
Perron et al. (2002)	Screening		Extent that increased incidence resulted in decreased mortality	Change rates between incidence and mortality not inversely related	Evaluation period only 1 yr. Quebec cancer registry uses in hospital discharge

Table 6: continued.

Author (year)	Risk Factor	Study type or datasets	Outcome measure	Finding (s)	Limitations
ERSPC (Europe)	Screening	Large RCT (on going)	Extent that early screening leads to reduced incidence and mortality	Final results not available. Hope to show that early screening leads to 25% reduction in mortality	Suspect selection bias, lead-time bias, and contamination bias. Over diagnosis and over treatment. Healthy men effect.
Draisma et al. (2003)	Overdetection and over treatment due to screening	Rotterdam section of ERSPC	Overdetection from screening leads to over treatment and unnecessary treatment	Men aged 55 had 27% overdetection rate and 12.3 yr. lead time Men aged 75 had a 56% overdetection rate. Dutch men should have greater than 1 yr. screening interval	Men limited to Dutch origin only No racial or ethnic groups included
Etzioni, Penson et al. (2002); Ciatto et al. (2004); Graif et al. (2007)	Overdetection and over treatment due to screening	Computer Modeling; Cohort from ERSPC	Magnitude of overdiagnosis and impact on unnecessary treatment	2 million men modeled 29% overdetection rates in Caucasian and 44% in African American (Etzioni), Ciatto and colleagues agreed overdiagnosis is prevalent 27% of men were found to have been underdiagnosed and only 5% overdiagnosed (Graif)	Same as noted within ERSPC

Table 6: continued.

Author (year)	Risk Factor	Study type or datasets	Outcome measure	Finding (s)	Limitations
Van Der Cruijsen-Koeter et al. (2005)	Prognostic factors associated with screened/control group	Rotterdam section of ERSPC	TNM staging and Gleason score	CDR[a]: 84% in screened group, 59% in control group. Distant mets: 7 men in screened group, 27 men in control group. Also 5x more likelihood for distant mets in control vs. screened group	Same noted within ERSPC and possible contamination rates
Raaijmakers et al. (2004)	PSA changes over 4 yrs. in men with and without prostate cancer	Rotterdam section of ERSPC	PSA sub forms: PSAV PSADT	Men with PCa[b]: PSAV=0.62ng/mL/yr. PSADT = 5.1yrs. Men w/o PCa: PSAV=0.46ng/mL/yr. PSADT = 6.1yrs.	Only had 2 PSA tests over short follow up period
Hugosson et al. (2004); Schroder et al. (2006)	Screening	Swedish section of the ERSPC	PSA at 2yr intervals over 8yrs (4 PSA tests)	PSA highly associated with increased risk in 1st screening round. Stage shifts make advanced disease and mets nearly non-existent in late screening rounds	Same noted within ERSPC
Kwiatowski et al. (2004)	CDR of prostate screening	Switzerland section of the ERSPC	CDR of PSA tested men	Out of 7,124 PSA tested men CDR = 2.5% Men with mets = 7% Final conclusion: did not recommend large screening programs	Same noted within ERSPC

Table 6: continued.

Author (year)	Risk Factor	Study type or datasets	Outcome measure	Finding (s)	Limitations
PLCO (U.S.)	Screening	Large RCT (on going)	Extent that early screening leads to reduced incidence and mortality	Final results not available	
Ford, Havstad, Demers, et al. (2005)	Screening	PLCO data	Effects of baseline false + results on men returning for second round screenings	Men 2x more likely not to return for second round (OR 1.96) when receiving an initial false + compared with men receiving an initial negative result Education was significant (OR 1.71 and) Age was not significant (OR 1.02)	Information obtained from participants in long-term screening trials may not be representative of population due to healthy effect. Results may not be generalized across other geographical regions.
Crawford et al. (2006)	Screening	PLCO data	Time for normal PSA values to convert to abnormal levels	1.5% of men with PSA <1.0ng/mL will convert to >4.0ng/mL in 5 yrs. 33.5% of men with PSA 2.0-3.0ng/mL will convert. 79% of men with PSA 3.0-4.0ng/mL will convert.	

Table 6: continued.

Author (year)	Risk Factor	Study type or datasets	Outcome measure	Finding (s)	Limitations
Pinsky et al. (2007)	Screening	PLCO data	Examination of the healthy volunteer effect on overall mortality and cancer-specific mortality	PLCO members when compared to NHIS[c] members tended to be: Better educated More physically active More likely to be married Less likely to smoke. In contrast, being AA, ever smoked, low education, lack of physical activity, and not married all were associated with increased mortality	Study excluded cancers as a mortality ratio computation. AA men under-represented at 4.4%
Ford, Havstad, Fields, et al. (2008)	Screening	PLCO data	Effects of comorbidities or number of comorbidities on adherence to RCT protocol	No significant differences between comorbidities. Only smoking showed negative statistical significance on adherence to the PSA test (less likely to adhere to protocol, OR 0.6). No racial differences, AA's with comorbidities as likely to participate as Caucasians	Sample included elderly AA men from a single geographical location (Metro-Detroit). Questionnaire did not include psychiatric comorbidities
Sandblom et al. (2004)	Screening	RCT pilot study	Feasibility of a large population-based screening program	Three year screening interval sufficient for early stage prostate cancer. Cost effective	Disparate mortality among race not studied. Small Population restricted to 1 geographical city (n = 9,026)

Table 6: continued.

Author (year)	Risk Factor	Study type or datasets	Outcome measure	Finding (s)	Limitations
Concato et al. (2001, 2006)	Screening	Nested Case-control	Association of mortality and PSA use	No evidence of screening benefit in matched case-control in overall mortality. Evidence did exist for PSA screening and cancer-specific mortality for African Americans	Race not matched initially. Race adjusted for in statistical analysis
Weinmann et al. (2004)	Screening	Case-control	Association of mortality on PSA and DRE use	Inverse relation found between PSA and DRE with cancer-specific mortality. 30% reduction in mortality	Not able to separate effects of DRE on PSA. Initial rise in PSA use during study period may inflate odds ratio
Weinmann et al. (2005)	Screening	Case-Control cohort from 4 HMOs	Association of mortality on PSA and DRE use	Use of PSA and DRE was associated with reduced mortality in Caucasians but not African Americans	Not able to separate effects of DRE on PSA. Low participation of African Americans. Possible misclassification bias.

Table 6: continued.

Author (year)	Risk Factor	Study type or datasets	Outcome measure	Finding (s)	Limitations
Etzioni, Berry et al. (2002)	Screening	SEER13 - Medicare Registry 1991-1998	Comparing PSA use among AA and Caucasian	AA less likely to use PSA. Variable testing patterns (i.e., Caucasians had higher PSA testing rates in areas of greater AA populations and less testing rates in areas of greater Caucasian populations)	Administrative claims data yield combined results from multiple areas. Heterogeneity across geographical regions is great in SEER-Medicare registries

a: CDR is cancer detection rate
b: PCa is prostate cancer
c: National Health Interview Survey

Caucasians. In addition, African American men are more commonly diagnosed at earlier ages than Caucasian men (mean 63.7 years versus mean 68.1 years).

From the NCI's SEER Cancer Statistics Review of 2000-2004 dataset, recall that the median age at diagnosis for all races with prostate cancer is 68 years with 36.2% included in the range up to 64 years; 36.7% in the range between 65-74; 22.4% in the range of 75-84; and 4.7% for ages over 85 years (NCI, 2008). The report also listed the median age of death due to prostate cancer in the United States to be 80 years during 2000-2004 with approximately 8% of deaths occurring for ages up to 64 years. The remaining 92% of deaths occurred after age 65 (NCI, 2008).

Some studies suggest that diets high in fat vary among different races and could possibly contribute to a higher risk of prostate cancer. For example, Japanese men living in Japan have a lower incidence rate and lower fatty intake in their diets than Japanese men living in the U.S whose levels of fat intake closely resemble those of Western men. Immigrant studies have shown that when Japanese men move to the United States their incidence and mortality rates increased to levels similar to American men. Further, screening in the United States is greater among Caucasian men than African American men that intuitively may suggest that incidence rates for Caucasians would be higher, yet the opposite is true. Although it is clear that many factors contribute to the different race-specific incidence rates, it is not clear as to what role these factors play on racial disparities. Factors such access to care, detection differences, differences in decision making, lacking communication processes between patient and physician, variable patterns of care, multiple treatment choices and options, genetics, and dietary differences

all contribute to the mixed results and limited knowledge gained to date (Bostwick, 2004).

Age has shown to increase a man's risk of developing prostate cancer. For example in men 80 years and over, the incidence of prostate cancer was 80% as confirmed by autopsy (Bostwick, 2004). A study on the international trends of prostate cancer-specific mortality found, that age-specific death rates increased with age for most of the 24 countries studied. Results indicated that in the United States alone, age-specific death rates from 1979 to 1999 varied from less than 5 per 100,000 for men 50-54 years to nearly 250 per 100,000 for men 75-79 years (Oliver, May, & Gunnell, 2001). Whereas men younger than 40 years rarely have prostate cancer, prostate cancer is widely observed in men 65 and older suggesting that it could develop as a result of damaged genes seen in older men (Bostwick, 2004).

Exogenous risk factors of prostate cancer include diet (weight and obesity), environmental agents, occupation, and physical activities. Different descriptive epidemiologic studies have shown that dietary factors may contribute to prostate cancer. However, not all studies of this type have reported the same association indicating again, that not all is clear when assessing risk and incidence of prostate cancer (Kolonel, 1996; Schuurman, Van den Brandt, Dorant, Brants & Goldbohm, 1999). For example, some studies have shown a positive correlation between incidence or mortality and fat intake in multiple countries including the United States. Many case-control studies have reported a positive association as well. However, few of those studies adjusted for energy intake and many reported differences in methodology (Heshmat et al., 1985; West, Slattery,

Robison, French & Mahoney, 1991; Whittemore, Kolonel et al., 1995; Rohan, Howe, Burch & Jain, 1995). Other studies differed in selection of controls and dietary assessment that resulted in selection bias issues and patient's weight and caloric intake were often ignored.

Some studies used quantitative parameters based on consumption of high fat foods such as meat and dairy products. One study found that the positive association disappeared when controlling for energy intake (Anderson et al., 1996). One clinical study examined the intake of antioxidants (e.g., herbal supplements and Lycopene found in tomatoes) to determine whether they had any protective properties against prostate cancer. Finally, other studies included dietary factors high in animal fat and low in fruits and diets high in Vitamin E and selenium again, examining their effects on prostate cancer (Bostwick et al., 2004; Prostate Cancer Initiative-CDC, 2007).

Alcohol and smoking have been associated with increased risk of prostate cancer. Alcohol may increase a man's metabolic clearance of testosterone, which could exhibit protective affects against cancer. However, most studies have found a significant link between alcohol and increased risk (Anderson et al., 1996; Slattery & West, 1993; Hayes, Brown, & Schoenberg, 1996; Dennis, 2000; Sesso, Paffenbarger & Lee, 2001). Hayes and colleagues (1996) found an elevated risk when men consumed between 2-6 drinks per week (OR 1.4; 95% CI 1.0-1.8). If men had greater than 6 drinks each week the risk increased by almost two times compared to men who never consumed alcohol (OR 1.9; 95% CI 1.3-2.7). A different study showed an inverse risk associated with heavy consumption of alcohol, although no biological explanation was given (Breslow,

Wideroff, Graubard et al., 1999). A Harvard Health Study found a positive association for increased risk of prostate cancer with moderate consumption of alcohol when drinking liquor and not beer or wine (Sesso et al., 2001). In contrast, a study in Montreal found that drinking beer was associated with an increased risk and drinking at a younger age also increased risk (OR 3.8; 95% CI 1.6-9.3) for boys who began drinking before age 15 (Sharpe & Siemiatycki, 2001).

In regards to smoking, a plethora of data exist demonstrating inconsistent and contrasting evidence for the association of smoking and risk of prostate cancer. Numerous case-control studies examining the association between smokers and non-smokers are reported but few have shown significant findings. Despite some studies demonstrating an increased risk in current and former smokers of greater than 40 cigarettes per day, the lack of consistent findings and the lack of dose response relationships argues against any causal association (Hayes, Pottern et al., 1994). Because of the conflicting and inconclusive evidence on smoking and prostate cancer, an international consensus conference in 1996 concluded there was inadequate data to associate smoking with increased incidence. However, a more recent case-control study did find a dose response relationship in men who had smoked greater than 40 pack-years. The study also reported that cessation of smoking was positively associated with a reduced risk in prostate cancer (Plaskon, Penson, Vaughan, & Stanford, 2003).

The effects of diabetes on prostate cancer risk have also been evaluated with a study in New York City finding that diabetics had a lower risk. However the lower risk was only associated with whites and Hispanics. Risk among African American men was

not affected if they were diabetic. It is believed that this may be due to black men generally having higher levels of testosterone and even though diabetes has a lowering effect on testosterone levels, it would not be sufficient to noticeably reduce risk (Rosenberg, Neugut, Ahsan & Shea, 2002).

Another exogenous risk factor includes environmental agents. Exposure to low levels of estrogen and other natural plant substances have been associated with increased risk of prostate cancer. Agents such as agricultural chemicals, plastics, detergents, and some dyes, such as Red Dye No. 3, all contain small levels of estrogen. Some products made from soybeans, whole-grain cereals, seeds, nuts, and berries are converted by intestinal acids into estrogen (Adlecreutz et al., 1995). Exposure to cadmium and certain pesticides have shown an increase risk for developing prostate cancer as well. Cadmium is an environmental contaminant found in zinc mining and sewage disposal areas making it an occupational hazard. Most of the cadmium mined in the U.S. is used for metal plating. Smaller amounts of cadmium are used for pigments, batteries, and stabilizing plastics. When used for industrial purposes cadmium concentrations in food, soil, and air can be dangerously high. For example, in a population-based study in Utah, occupational exposures to cadmium showed a small increase risk for developing prostate cancer (Elghany, Schumacher, Slattery, West & Lee, 1990). In addition to being an occupational hazard, cadmium exposure may result from eating fish, drinking water, and smoking (Faroon, Williams, & O'Connor, 1994; Waalkes, Rehm, Parantoni, & Coogan, 1992) (see Table 7).

Table 7. Summary of Studies Evaluating Risk and Prostate Cancer.

Author (year)	Risk Factor	Study type or datasets	Outcome measure	Finding (s)	Limitations
Bostwick et al. (2004); USPSTF[a] (2002)	Family history	EPA report	Family history and risk of developing prostate cancer	Men are 2 to 3 times more likely to develop prostate cancer when 1st degree relative have it	Report may contain selection bias as clinical and pathological features of familial and non-familial can be similar
Whittemore et al. (1995)	Family history	Unknown	Family history and risk	AA men with family history have almost 2x higher risk than Caucasian (OR 1.9)	Numbers not statistically different
Cotter et al. (2002)	Family history	Unknown	Family history and risk	31.2% of AA men and 22.2% of Caucasian men reported having family history	None listed
Bostwick et al. (2004); CDC[b] (2007)	Male hormones	Report	Testosterone and androgen and risk	High levels of testosterone might increase a man's risk over time. Hormones may affect cancer growth and progression	Results inconsistent to confirm any relationship.

Table 7: continued.

Author (year)	Risk Factor	Study type or datasets	Outcome measure	Finding (s)	Limitations
Bostwick et al. (2004); NCI[c] (2008)	Race/ Ethnicity	Report	Race and risk	AA men 1.6 times more likely to present with advanced stage and with mets and 2.4 times more likely to die than Caucasians	None listed
Oliver et al. (2001)	Age	Observational International study of 24 countries	Age and risk	Increased age increases likelihood of developing prostate cancer. Death rates reported from1979-1999 5/100k in aged 50-54yrs 250/100k in aged 75-79yrs	None listed
Kolonel (1996); Schuurman et al. (1999)	Diet (weight and obesity)	Descriptive epidemiologic	Fatty dietary intake	Shown mixed results for positive association between mortality and fatty diet intake	Not all studies have shown similar results indicating variable methodology and design. Selection bias, low response rates

Table 7: continued.

Author (year)	Risk Factor	Study type or datasets	Outcome measure	Finding (s)	Limitations
Anderson et al. (1996); Slattery & West (1993); Hayes et al. (1996); Dennis (2000); Sesso et al. (2001); Sharp & Siemiatycki (2001)	Alcohol	Observational Case-controls	Alcohol consumption and increased risk	Elevated risk for men consuming 2-6 drinks per week (OR 1.4). Men having >5-6 drinks/week risk increased ~2x (OR 1.9). Increase risk found for liquor not wine or beer. Contrasted by an increase in risk when drinking beer and drinking at earlier age (OR 3.8 for boys beginning to drink before age 15)	No definitive link could be found due to mixed results
Hayes et al. (1994); Plaskon et al. (2003)	Smoking	Case-control	Smoking and increased risk	Few studies finding significance. One found increased risk and smokers of 40 cigarettes per day. Another found reduced smoking was associated with a reduced risk	Inconsistent and contrasting evidence indicating lack of support

Table 7: continued.

Author (year)	Risk Factor	Study type or datasets	Outcome measure	Finding (s)	Limitations
Rosenberg et al. (2002)	Diabetes	Observational	Diabetes and race on risk	New York study found diabetes has a lowering risk effect on Caucasians and Hispanics but not for AA men	None listed
Adlecreutz et al. (1995)	Environmental agents containing low levels of estrogen	Unknown	Chemicals, plastics, detergents, red dye no.3,	Exposure to these agents have shown small association with increased risk	None listed
Elghany et al. (1990)	Cadmium and some pesticides	Unknown	Cadmium	Cadmium is found zinc mining and sewage disposal areas. Also in pigments, batteries, and plastics. Exposure has shown increased risk	None listed

a: U.S. Preventive Services Task Force
b: Centers for Disease Control - Prostate Cancer Initiative
c: National Cancer Institute – SEER cancer statistics review

Incidence and Prostate Cancer-Specific Mortality

A summary at the end of this section details the studies on incidence and mortality reviewed in this chapter. In the early 1990s when screening with the PSA test began to increase, changes in prostate cancer incidence and mortality were observed both in the U.S. and internationally (Oliver, May & Gunnell, 2001; ACS, 2008). Incidence rates of prostate cancer in all races in the U.S. increased gradually from 1988 through 1992, then declined sharply until 1995 at which time they began to rise again slowly. The ACS attributes these trends to prostate cancer screening with use of the PSA test and a DRE. They suggested that the rising incident rate after 1995 was due to increased prostate screening based on emerging screening guidelines in men less than 65 years old. According to the National Cancer Institute's SEER registries, incidence rates rose from 112.7 and peaked at 190.1 per 100,000 men between the years 1989 and 1992 adjusting for annual age (Mettlin, Murphy, Rosenthal & Menck, 1998). Since the peak year of 1992, rates declined each year thereafter to a level of 144 per 100,000 in 1994. The authors concluded that the pattern of incidence rates were a result of increased screening interventions. Data from SEER showed a dramatic increase in age-adjusted incidence near the same time. The data showed an increase by 20% each year from 1989 to 1992, after which rates decreased by almost 11% per year until 1994 where they stabilized.

Mortality trends paralleled incidence rates in that during the late 1980s, the annual percent increase in the U.S. rose from 0.7% to 3.1% for Caucasian men and from 1.6% to 3.2% for African American men. These rates began to decline in 1991 for Caucasians

dropping nearly 22% from 1991 to 1999 and decreasing 16% from 1993 to 1999 for African Americans (Harris & Lohr, 2002).

In the United Kingdom, mortality trends were analyzed using the World Health Organizations (WHO) Mortality database for 1979–1997. Twenty four countries were evaluated using age-standardized death rates for men aged 50–79 years grouped into 5-age categories (Oliver et al., 2001). Results from the United Kingdom study showed a greater than five-fold difference between the country with the lowest mortality rate (Japan with 15.1/100,000 men) and the country with the highest mortality rate (Sweden with 81.5/100,000 men). The U.S. was found to be a country with a high mortality rate during the 1990s. Although not included, the authors noted that mortality rates in the U.S. increased 1%-2% each year during the PSA era (1986-1992) and then declined sharply through the end of 1997.

Of note, the United Kingdom study found that in countries where the PSA test was commonly performed, (U.S. and Austria) mortality rates decreased. Interestingly, the United Kingdom itself, a country with low PSA use, also experienced decreasing mortality rates. Additionally, results from the Tyrol region of Austria showed a decreasing mortality where PSA was free to all men of that region; however, no other region within Austria experienced a decline (Oliver et al., 2001).

A similar study from the International Agency for Research on Cancer (IARC) using the SEER registries, examined age-standardized mortality rates from 15 countries over a 20 year period (Hsing, Tsao & Devesa, 2000). Results also found the U.S., among other countries, as a country having high mortality rates (Hsing et al., 2000). The study

also noted that African American men in the U.S. had the highest mortality rate of all at 50-60 times higher than the lowest rates seen in Shanghai, China. Caucasians within the U.S. were found to have the second highest of all men (Hsing et al., 2000).

In examining race and incidence and mortality, African American men in the U.S. are 1.6 times more likely to develop prostate cancer than Caucasians (258.3/163.4 rates per 100,000 age-adjusted to the 2000 U.S standard population). Additionally, African Americans are 2.4 times more likely to die from prostate cancer than Caucasians with 64 deaths to every 26.2 deaths per 100,000 age-adjusted to the 2000 U.S. standard population (ACS-AA, 2007/2008). Reasons for these differences remain unclear. Factors such as late stage, higher disease grade, and less screening interventions may influence treatment strategies contributing to differences in mortality rates. To address these differences, a study to evaluate prostate incidence, mortality, and survival among African American men and Caucasian men was performed (Chu, Tarone & Freeman, 2003). The authors used data from the SEER registry of 1975-1999. Mortality rates were calculated from death certificates from the National Center for Health Statistics. All men in the study were divided into the following seven age groups. The study showed a decline in mortality beginning in 1990 for both races. However, the authors concluded these declines were mainly attributed to changes in medical practice patterns and not changes in prostate cancer risk factors (Chu et al., 2003). Moreover, the results showed that the declining mortality rates indicated a decline in deaths of men who had distant metastasis. Men with localized disease did not exhibit reductions until 1997. In addition, the declining mortality rates were greater among Caucasians compared with African

Americans. Disparate mortality rates between races remained high. For example, the mortality rate for Caucasians decreased to approximately 52 men per 100,000 whereas the rate settled at 100 African American men per 100,000 in 1999. The authors offered no explanation other than the fact that the number of Caucasian men receiving prostatectomy during the period was higher compared to African American men. These differences may reflect different treatment strategies either offered to or chosen by African American men (Chu et al., 2003).

A study using SEER data from the three states of Connecticut, Iowa, and New Mexico examined prostate cancer mortality among African American men in relation to the PSA test. The authors noted that of the five states within the SEER registry at the time of their study, these three were the only ones with sufficient numbers of deaths of African American men needed to make reliable mortality rate estimates (Escobedo, Rivas & Holmes, 2004). The study included three time periods, 1979-1986 (before PSA use), 1987-1990 (during PSA use), and 1991-1998 (after introduction of PSA test). The results showed an increase in mortality in Connecticut and Iowa and a decrease in mortality in New Mexico. In particular, Connecticut reported an increased annual percent change (APC) from the "before PSA" period to each of the other two periods by +4% and +20% respectively. Iowa reported an increased APC from the first period to the other two periods of +40% and +18% respectively. New Mexico reported a decrease in mortality in the last two periods compared with the first period of -41% and -55% respectively. The authors noted that during the study period changes in treatment procedures emerged and in fact, were different for New Mexico as compared to the other two states. For example,

the number of men receiving prostate surgery was five times greater in New Mexico than in Connecticut and Iowa, which could partially explain the decrease in mortality in that state. The authors were unable to assess the role that quality of care played in the three states while admitting that use of definitive treatments may have influenced observed mortality patterns. Further, PSA utilization was greater in Connecticut and Iowa than New Mexico whereas prostatectomy was used far more often in New Mexico. The authors felt that the limited adoption of the PSA test in New Mexico may have been due to barriers to access in a large land mass state with large numbers of men who were uninsured.

Additional limitations included the fact that the SEER data of that time had not yet been linked to Medicare claims data; therefore, they could not assess socioeconomic factors and cancer burden regarding social classes. In addition, small sample sizes limited their ability to assess the impact of treatment strategies of curative intent over time. The study did not include data on comorbidities which may play a role in mortality statistics as well (Escobedo et al., 2004).

A different study assessing racial differences in mortality showed similar results. The study consisted of a cohort of 4,686 men during 1980-1997 from the Henry Ford Health System cancer registry and examined differences in surgical use and the extent to which these differences were associated with disparate survival rates between African Americans and Caucasians (Tewari, Horninger et al., 2005). Three hypotheses were considered in the study, 1) that differences exist in stage and grade between African Americans and Caucasians, 2) African American men receive surgery less often than

Caucasians, and 3) that differences in survival between African Americans and Caucasians could be explained by differences in surgery rates and other confounders.

Their results showed that overall, African American men were older, had higher Charlson comorbidity indices, had shorter follow-up periods, had lower incomes, and chose surgery less often than Caucasians (Tewari, Horninger et al., 2005). The multivariate analysis indicated a moderate association between poor survival and higher grade disease, older age, comorbidities, and lower income ($p = 0.013$). The authors noted that after adjusting for race, no difference in cancer-specific mortality existed ($p = 0.29$). In all cases, survival was better for Caucasians until adjusting occurred which tended to reduce or eliminate racial differences. The study reported that of all confounders, income (An SES component) explained 50% of the differences while treatment could account for approximately 34% of the differences in survival between African Americans and Caucasians (Tewari, Horninger et al., 2005). The authors concluded that more aggressive treatments such as prostatectomy and radiation therapy should be provided to African Americans in order to help reduce the disparity in mortality.

Limitations of the study as noted by the authors included several potential biases. Of note, the treatment selection process in that treatments offered most often depend on which specialist the patient consults For example, urologists might suggest the patient have surgery whereas the radiation oncologist might offer radiation therapy or brachytherapy as the best treatment choice. The specialists may also choose younger healthier patients in order to influence better outcomes. Further, the authors noted that treatment technologies have improved and the fact that men are generally healthier and

thus live longer could influence differences in mortality as well. Strengths of the study were also reported and include sufficient numbers of African American men existed (41%) within the Henry Ford Health System, and therefore, a representative sample participated. In addition, the authors believed that using only the biopsy result for tumor grading in all treatment strategies helped protect against under-grading, a bias effect seen in other similar studies that used two different tumor grading systems. The two were biopsy score*s* for men receiving conservative management and radiation therapy and the surgical pathology score for the surgery patients. Obviously, a more accurate grade is achieved when the prostate gland is removed allowing for a more complete and thorough pathological exam.

A study from 2004 was performed to try and explain racial differences in prostate cancer mortality among races. The authors examined SES factors, attitudes toward the health care industry, dietary factors, and outcomes after treatments (Freedland & Isaacs, 2005). They reviewed much of the existing literature and found that when studies were adjusted for stage, grade, PSA and treatment received by the patient, African Americans and Caucasians had similar outcomes. It was concluded that the main contributing factor for racial disparities noted in these observation studies was most likely due to SES factors (Freedland, et al., 2005). For example, men's perceptions about health and knowledge about prostate cancer screening were found to be highly dependent upon education and income levels. It is also known that African American men do not participate in screenings as often as Caucasians. Reasons for lower screening rates are plentiful and include minority status and lower socioeconomic status, limited access to care, often

distrust of the medical community, coping with disease, depression, and many others (Freedland, 2005; Marion & Schover, 2006).

It is known that racial disparity exists in the care and the outcomes associated with prostate cancer. However the reasons for disparity still remain unclear. In two studies from 2000, authors evaluated whether African Americans were still more likely to die from prostate cancer after adjusting for confounders such as socioeconomic factors (SES). Socioeconomic factors were measured using ecologic variables at the census-tract level as well as covariates of stage, grade, age, comorbidities, and treatments to try and resolve the disparity (Robbins, Whittemore & Thom 2000; Merrill & Lyons, 2000; Du et al., 2006). Robbins and colleagues (2000) examined the extent of SES differences as measured at the census-tract level that accounted for racial differences in two end points of prostate cancer-specific mortality and overall mortality among men with prostate cancer. The study included men from the San Francisco Bay area within the SEER registry from 1973–1993. The study included only ecologic factors associated with SES because SEER data does not provide individual level data, only census-tract level (Robbins et al., 2000). Therefore, the study resulted in 1005 census tracts containing 23,334 men. For each of the 1005 census tract levels, data were obtained from the 1990 U.S. Census of Population and Housing Summary Tape File 3A (17). Robbins and colleagues (2000) obtained only two variables, percent of adult residents with a minimum of a high school education or higher and the percent of families below the poverty line. The authors believed that these two components were the most important in terms of health outcomes (Robbins et al., 2000). Cause of death was obtained from death

certificates. Out of the 23, 334 men in the study 19,996 were Caucasian and 3,338 were African American. The results showed that African American men were diagnosed at earlier ages, had lower SES status, and had a greater probability of presenting with higher stage and grade disease. The results also showed that after adjusting for age and stage, African American men were still 1.25 (95%CI; 1.14-1.37) times more likely than Caucasians to die from prostate cancer and when adjusting for SES factors, the death rate ratio decreased only slightly to 1.2 (95%CI; 1.07-1.35). The findings also indicated that African American men were only slightly less likely to obtain surgery than Caucasian men with absolute differences being only 7% (63.9%-56.9%) therefore the authors noted a negligible effect when adjusting for treatment received by both races (Robbins, 2000). They concluded that because the racial difference in death due to prostate cancer and SES factors was only minimal, that perhaps the risk is more closely associated with biological factors such as tumor virulence (Robbins, 2000).

Merrill and Lyons (2000) evaluated the same end points examining whether African American men were more likely to die of prostate cancer than Caucasians once controlling for age, stage, grade, comorbid conditions, and treatment. A major objective covariate for monitoring progress of disease is age-adjusted mortality rates (Merrill & Lyons, 2000). However, Merrill believed that it may be more sufficient to examine mortality in partitions where cause of death has been monitored from when the disease was diagnosed. For example, they believed that mortality portioned by calendar years would allow for longer evaluation periods in which vital signs and cause of death could be associated to disease at diagnosis (Merrill & Lyons, 2000). Further, they evaluated

data from the SEER registry database linked to Medicare claims information because this registry links mortality rates to factors associated with disease at the time of diagnosis which is referred to as incidence-based morality (IBM). For example, Merrill and Lyons (2000) illustrated the IBM method by describing a case of tracking a man diagnosed with localized prostate cancer at age 65 in 1980 and who would not have been previously diagnosed with any other cancer. He suggested the man was treated with radiation therapy and then died in 1988. If this man was listed in the SEER registry, he would have been tracked from the time of his initial diagnosis until his death and then his death could be characterized by the factors associated with his disease at diagnosis. All men within Merrill's study were identified and followed with this IBM method (Merrill & Lyons, 2000). This approach was considered useful in that the IBM method takes mortality and looks back in time to identify variables associated with disease at diagnosis thus giving the advantage of greater insight into the observed mortality rates (Merrill & Lyons, 2000). The SEER registry available at the time included data linked from 1973 through 1995 from five states (Connecticut, Iowa, Mew Mexico, Utah, and Hawaii) and four metropolitan areas including Atlanta, San-Francisco-Oakland, and Seattle-Puget sound. The age categories included all ages, 50-59 years, 60-69 years, 70-79 years, and over 80 years. Logistic regression analysis was used and odds ratios were calculated at the 95% confidence interval. Mortality rates were determined from deaths due to prostate cancer occurring 0 to 1 years within diagnosis, 0 to 2 years from diagnosis, up to 0-22 years since diagnosis.

The results showed that most prostate cancer IBM occurred during the 0 to 4 years of diagnosis (Merrill & Lyons, 2000). As other studies have shown, Merrill and colleagues (2000) also found that most men in their study died with prostate cancer rather than from the disease itself (Merrill & Lyons, 2000). Their results were also comparable to other studies showing that African American men were approximately twice as likely to die from prostate cancer as Caucasian men were during 1988–1995. They also noted that African American men were about 1.6 times more likely to die from non-prostate cancer causes than Caucasians were. Each variable was added to the race-model one at a time from most significant to least. All factors between races had an effect on prostate cancer mortality with late stage disease having the greatest effect showing an increased likelihood of African Americans to die from prostate cancer with odds ratio of greater than 5.0 for each of the four year groups reported. However, only race-grade interactions for the years 1992-1993 and 1994-1995 were significant (Merrill & Lyons, 2000). A limitation noted in the study was that IBM rates may contain lead-time bias (bias found when a screening test advances the time of diagnosis without advancing the time of death). However, it was noted that when using death rates as reported on death certificates, lead-time bias is usually removed. Merrill and Lyons (2000) noted the IBM method to be a strength of the study because they used a 0-7 year period that closely mimicked death certificate trends (Merrill & Lyons, 2000).

A 2006 study by Du et al. evaluated racial disparity and SES status among race and found similar results. The study used SEER-Medicare linked files from the eleven SEER areas and included 61, 228 men diagnosed with local/regional stage prostate

cancer. The SEER-11 registry included metropolitan areas of San Francisco/Oakland, Detroit, Atlanta and Seattle, Los Angeles County, the San Jose-Monterrey area, and the states of Connecticut, Iowa, New Mexico, Utah, and Hawaii representing greater than 14% of the U.S. population (Du et al., 2006). Of the 61,228 men, 53,764 were Caucasian, 6,321 were African Americans, with the remaining being of Hispanic descent.

Outcome variables (dependent) were survival time in months (defined from date of diagnosis to date of death), all-cause mortality (defined as death from any cause and as identified in SEER), and prostate-specific mortality (defined as men dying of prostate carcinoma) (Du et al., 2006). Independent variables included SES factors (defined by SEER as education, poverty, and income), a comorbidity index assessed from Medicare claims by diagnosis or procedures performed one year prior to and one month after being diagnosed with prostate cancer. Other independent variables included treatments received by the men and as defined either from SEER data codes or Medicare claims data. These included surgery, radiation therapy, and hormones. Demographic data on age, race, AJCC staging, pathological grade, year of diagnosis, and geographic area were also obtained.

Results indicated only slight differences in the proportions of men receiving any of the three treatment variables listed. For example, 23.9% of African Americans received hormone therapy compared with 27% of Caucasians and 28.7% Hispanics. The proportion of African American men receiving surgery or radiation therapy was 57.3% compared with 64.3% Caucasians and 59.6% Hispanics.

Regarding the SES status, 73.4% of African American men fell within the lowest quartile compared with only 60.6% Hispanics and 17.9% Caucasians (Du et al., 2006). In

terms of race and prostate specific mortality, the final adjusted model showed differences but no significant interactions with African American men being 17% (Hazards Ratio[HR]: 1.17) more likely and Hispanics being 22% (HR: 0.78) less likely to die from prostate cancer than Caucasian men. The hazards ratios for African American men increased slightly when adjusting for education (HR: 1.2), income (HR: 1.18), or poverty (HR: 1.19) when compared with Caucasians. These results indicate that in men with the same Medicare coverage and with the same disease stage of localized cancer, African American men were more likely to present with higher grade disease. However, the differences in mortality between races as noted in the study were reduced if not eliminated when adjusting for SES status (Du et al., 2006).

Other studies examining racial differences in survival and mortality after treatment for prostate cancer have been reported (Godley et al., 2003; Zeliadt, Potosky, Etzioni, Ramsey & Penson, 2004; Peters & Armstrong, 2005; Zeliadt et al., 2006; Richert-Boe et al., 2008). For example, Godley and colleagues (2003) examined men with prostate cancer from 1986 through 1996 from five SEER regions. These areas included Atlanta, Connecticut, Detroit, San Francisco, and Seattle mainly because these regions included sufficient numbers of African American men (Godley et al., 2003). Out of an initial 104, 537 men, the number remaining after removing those who did not meet study criteria was 43, 989. The study evaluated three endpoints, overall survival, non-prostate cancer-specific survival, and prostate cancer-specific survival. Treatment outcomes were assessed using Kaplan-Meier survival curves and Cox regression models. The survival curves were used to analyze racial comparisons within treatment groups and

PSA testing eras (the pre-PSA era of 1986-1989, the early PSA era of 1989-1991, and the recent PSA era of 1992-1996). Other independent variables including SEER site, census tract education and income level, age at diagnosis, PSA testing era, tumor grade, race, treatment, and comorbidity scores were all assessed using Cox regression models. All statistical tests were two-sided and tested at an alpha of 0.05 (Godley et al., 2003).

SEER staging definitions were based on clinical information and not on surgery; therefore for those men receiving prostatectomy, a possible misclassification bias existed because men initially classified as having localized disease could be upstaged to advanced disease once pathological findings were reported. This bias does not exist for men receiving radiation therapy and watchful waiting (Godley et al., 2003). To account for this potential bias, the authors classified all men having surgery as having localized disease because surgery is usually not indicated for advanced disease (Godley et al., 2003). Race was classified from both SEER and Medicare claims and was either "black" when reported black from either source with a 96% agreement and as "white" when classified as white without black and non-Hispanic with a 93% ascertainment agreement (Godley et al., 2003).

The study consisted of 38,242 (87%) Caucasian men and 5,747 (13%) African American men, all of whom differed significantly across most variables. For example, African American men were more likely to be 65-69 years old and less likely to be married. In addition, African American men were more likely to live in a census tract area where 25% of the residents had less than a high school education or in one where the household income was less than $23,000. Moreover, African American men were less

likely to have surgery and instead, were more likely to have chosen watchful waiting (Godley et al., 2003). The results further showed that survival was statistically significantly longer for Caucasians than for African Americans and when stratified by treatment, the disparity in survival was greatest for men receiving surgery and lowest for men receiving radiation therapy. For example, the study measured hazards ratio (HR) for each available treatment compared with death due to prostate cancer and found a HR of 1.43 (95%CI: 1.29 to 1.58) among African American men receiving surgery relative to Caucasian, a HR of 1.12 (95%CI: 1.03 to 1.22) for African American men receiving radiation therapy, and a HR of 1.19 (95%CI; 1.12 to 1.26) for African American men receiving watchful waiting (Godley et al., 2003). The results also indicated that among surgery patients African American men died on average 1.8 years before Caucasian men and only 0.7 years and 1.0 year before those who received radiation therapy and watchful waiting respectively. Racial disparities still persisted after adjusting for all covariates as well.

The authors concluded that among surgery patients, African American men between the ages of 65 and 84 have poorer survival rates with highest mortality rates than do Caucasian men compared to radiation therapy and less aggressive management. Possible explanations included reduced access and other social, environmental, and biological factors that may have played a role. Response to treatment due to genetic differences between races was also given as a possible reason for the observed disparity observed. Limitations of the study included not knowing tumor size and not having information on serum PSA levels. Further, SEER only provides census tract level data

and not individual level data for socioeconomic factors which could contribute to higher levels of misclassification and therefore not allowing for accurate estimates of income and education levels (Godley et al., 2003).

Zeliadt and colleagues (2004) evaluated trends in men with localized prostate cancer using SEER registry data as well, noting that from a cohort of 90,128 men from 1991 to 1999, African American men were 26% less likely to receive aggressive curative treatments than Caucasians. By 1999, use of hormone therapy (ADT) had begun to increase, however, African American men who chose conservative management (watchful waiting) were still less likely to be treated with ADT with 35.8% receiving hormones compared with 45.6% Caucasians receiving hormones (Zeliadt, Potosky et al., 2004). The study found a significant racial disparity in the use of adjuvant hormone therapy (receiving hormones concurrently with radiation). The authors noted this as troublesome because recent studies have shown survival benefits when hormones are combined with radiation, especially when African American men typically present with advanced disease that would indicate hormone therapy.

Peters and Armstrong (2005) reviewed the literature from 1992 through 2002 and in 2005, reported finding only 27 articles that matched their inclusion criteria. However, 79% of those articles resulted in no significant racial differences in treatment outcomes. The remaining 21% found worse outcomes among African Americans in 5-year survival and rates of PSA failure (Peters & Armstrong, 2005). On the basis of their review, the authors noted that if African American men receive the same care and treatment as Caucasian men, no differences in outcomes were observed. There are many contributing

factors of why in spite of this, that African Americans present with higher grade disease and higher PSA levels. The authors concluded that perhaps efforts to increase or improve community PSA screening utilization to associate the racial differences noted may need to be addressed (Peters & Armstrong, 2005).

In the study by Richert-Boe and colleagues (2008) an attempt to further explain racial differences in treatment outcomes was undertaken. They evaluated groups of men from the Kaiser Permanent Northwest (KPNW) which is a Health Maintenance Organization (HMO) located in Oregon and Washington State. One group consisted of all available men (both races) receiving treatment with curative intent (TCI), diagnosed with localized disease and matched on age, stage, and grade using logistic regression. In a different group, men were separated by race where African American men (n = 79) were individually matched to 158 Caucasian men on age, tumor grade, and year of diagnosis. The results showed that of group one, 3,040 Caucasian and 79 African American men met inclusion criteria with 82% of Caucasian men and 71% of African American men receiving TCI. Once all covariates were controlled for, African American men were less likely to receive TCI than Caucasian men ($p = 0.01$) (Richert-Boe et al., 2008).

Of men of group two that were matched on all observed covariates, 56 African American men and 136 Caucasian men received TCI. Again, after adjusting for all covariates, African American men were less likely to be treated with TCI than Caucasian men ($p = 0.02$) and less likely to be offered TCI than Caucasian men ($p = 0.004$). The authors noted that these differences were not a result of lack of insurance as all men had similar coverage by being members of the same HMO; however, they did explain that

other factors such as limited transportation, job flexibility, access, and home support could have played a role (Richert-Boe et al., 2008).

Summary of Literature Review

This chapter provides an extensive review of multiple studies concerned with prostate cancer screening and disease-specific mortality among race, including two large randomized clinical trials currently underway in the U.S. and Europe. The enormous task of associating the value of PSA screening with reduced mortality as well as narrowing the racial gap between African Americans and Caucasians remains untold. There are known factors discussed in these reviews that make up racial disparities and those factors not yet discovered that are convoluted in ways that may never be explained. Therefore, research should not be limited to usual and customary reviews but, instead, should explore new innovative processes applied to real clinical practices in search of answers. In addition, there are common themes emerging throughout the literature that should be investigated in order to resolve complications such that progress can be made to eliminate health care inequalities. One such theme includes increased mortality rates among African American men with localized prostate cancer who tend to present with advanced grade and stage disease at diagnosis. Differences in treatment management and socioeconomic factors were also well documented. Most studies evaluated outcomes of cancer-specific mortality after adjusting for covariates of stage, grade, age, race, SES factors, comorbidities, and treatments. Because of the significance found in other studies, this study will include all the same variables into a robust method using the propensity scoring analysis to evaluate their effect on cancer-specific mortality (see Table 8).

Table 8. Summary of Incidence and Mortality Studies.

Author (year)	Study Category	Study type or datasets	Outcome measure	Finding (s)	Limitations
Mettlin et al. (1998); ACS (2008)	Mortality/Incidence trends	NCI-SEER registries	Mortality and incidence trends in U.S.	U.S. incidence rose from 112 to 190/100k from 1989-1992. Incidence dropped to 144/100k by 1994. Mortality trends paralleled incidence	None listed
Oliver et al. (2001)	Mortality trends	WHO[a] mortality database	Mortality trends from 24 countries in United Kingdom	>5x difference in country with highest (Sweden 82/100k) and country with lowest (Japan 15/100k) mortality rate. Noted correlation between PSA and decreased morality in countries performing the PSA (U.S. & Austria). Found decrease in mortality in U.K with low PSA use.	None listed
Hsing et al. (2000)	Age-standardized Mortality	IARC[b] and SEER registries	15 countries over 20 yrs.	AA men in U.S. have highest mortality rates of all at 50-60 times higher than the lowest rates in China. Caucasians in U.S have second highest	None listed

Table 8: continued.

Author (year)	Risk Factor	Study type or datasets	Outcome measure	Finding (s)	Limitations
Collin et al. (2008)	Age-specific mortality trends in U.S. and U.K.	Data from Cancer Research UK, London UK and Seer registry in U.S.	Mortality trend comparison of both countries	Mortality rates similar in both countries and peaking in 1990s. Trends diverged (separated) in 1994. U.S. APC[c] ↓@ 4% ea.yr. U.K. APC ↓@ 1% ea.yr.	None listed
Chu et al. (2003)	Incidence, mortality, and survival in AA and Caucasian	SEER registry from 1975-1999	Race-based incidence, mortality, and survival	Decline in mortality beginning 1990 for both races due to practice pattern changes not risk factors. Decline was greater in Caucasians. Racial disparate mortality rate high (i.e. by 1999 rate at 52/100k in Caucasian and 100/100k in AA	None listed
Escobedo et al. (2004)	Mortality and PSA associations among AA men	SEER-registry from 3 states Connecticut Iowa, and New Mexico	3 time periods of 1979-1986 1987-1990 1991-1998	Increased mortality in Connecticut, Iowa. Decrease in New Mexico.	Treatment options changed during periods. PSA use greater in Connecticut and Iowa. Surgery given more often in New Mexico SEER not linked with Medicare (at that time). Small sample size. No comorbidity data.

Table 8: continued.

Author (year)	Risk Factor	Study type or datasets	Outcome measure	Finding (s)	Limitations
Tewari et al. (2005)	Mortality: racial differences	Henry Ford Health System's cancer registry	Surgery differences among races and the effects in survival of 4,686 men from 1980-1997.	AA men were older, higher comorbid index, shorter follow-up periods, lower income, had surgery less often than Caucasians. Adjusting for race, no significant differences in mortality (P=0.290). Income (SES component) showed highest relationship explaining 50% of differences.	Treatment selection bias (urologist push surgery, radiation oncologist push radiation and brachytherapy) Physicians likely to choose healthier patients to improve outcomes.
Freedland & Isaacs (2005)	Mortality	Literature review	Racial differences	When studies adjusted for age, grade, PSA, and treatment AA and Caucasians had similar outcomes. Main factor possibly SES based	None listed
Robbins et al. (2000)	Mortality	SEER registry 1973-1993 San Francisco Bay area	Extent that SES differences explained racial differences in mortality	AA men diagnosed at earlier ages, had lower SES status, and greater stage and grade. Concluded that racial differences in mortality only minimally attributed to SES	None listed

Table 8: continued.

Author (year)	Risk Factor	Study type or datasets	Outcome measure	Finding (s)	Limitations
Merrill & Lyons (2000)	Mortality	SEER-Medicare linked registry 1973-1995.	Used IBM[d] method to evaluate mortality	Most IBM deaths occurred at the 0-4 yr. since diagnosis time frame. Found a >5 OR for AA men for the factor "late stage"	IBM rates may contain lead-time bias.
Du et al. (2006)	All-cause mortality, survival, and prostate-specific mortality versus treatment	SEER 11 registry linked to Medicare	Racial disparate mortality	In men with same Medicare coverage and same disease stage, AA men more likely to present with higher grade (OR 1.17) than Caucasians. No difference when adjusted for SES	None listed
Godley et al. (2003)	Survival and mortality	SEER 11 cities with well represented AA populations	Survival/ mortality versus treatment and PSA testing between racial groups	AA men more likely to be older and choose watchful waiting, have less education, less often married, less likely to have surgery. **Mortality vs. treatment**: AA HR1.43 for surgery, HR1.12 for radiation, and HR1.19 for watchful waiting. Survival: AA men receiving surgery died 1.8 yrs. before Caucasians	Potential misclassification bias. SEER only has census tract level SES data (not individual). Unknown tumor size Unknown PSA levels.

Table 8: continued.

Author (year)	Risk Factor	Study type or datasets	Outcome measure	Finding (s)	Limitations
Zeliadt et al. (2004)	Trend analysis	SEER data from 1991-1999	Treatment trends among race	AA men OR 0.74 for aggressive treatment, less likely to have ADT[e] compared with Caucasians	None listed
Peters & Armstrong (2005)	Literature review	Articles from 1992-2002	Treatment outcomes among race	79% of articles reviewed showed no significant racial differences in treatment outcomes. The other 21% showed poorer survival and higher PSA failure rates among AA men	None listed
Richert-Boe et al. (2008)	Group analysis	HMO from Kaiser-Permanente Northwest	Racial differences in treatment outcomes	AA men less likely to receive TCI[f] (P = 0.01) and less likely to be offered TCI (P = 0.004)	Possible lack of access issues and lack of home support

a: World Health Organizations
b: International Agency for Research on Cancer
c: annual percent change
d: incidence-based mortality defined by SEER registry: monitoring a man from diagnosis through death enables longer evaluation periods capturing vital signs and cause of death that could be associated with disease at diagnosis.
e: adjuvant hormone therapy
f: treatment with curative intent

CHAPTER 3: METHODOLOGY

Introduction

This chapter begins with a brief examination of the theory of the propensity scoring method with presentation of a few medical research applications. A description of common quality assessment tools to evaluate the effectiveness of balancing covariates used for the propensity scoring method is provided including graphical displays. Next, discussions of the data source including selection and exclusion criteria are provided. Then, a description of the analytic approach is provided including conceptual model guidance, research methodology, study variables, and hypothesis testing utilized for answering the primary aim of the study; to evaluate what effects screening PSA may have on racial disparate mortality rates among African American and Caucasian elderly men. In particular, examination of influential predictors of prostate cancer-specific mortality commonly seen from screening PSA is given. Finally, a description of the study limitations is provided.

Theory of the Propensity Score

The propensity score is a form of matching on groups in an attempt to balance or remove differences on a set of observed covariates in observational studies. Using observational data to estimate treatment effects may lead to large differences in subjects causing selection bias issues. When selection bias is due to unobserved variables, Controlling for the bias is difficult and even controversial. However, when bias is due

to observed variables, traditional methods for controlling the bias are available. Multivariate matching of covariates is one method that may help to correct for differences in observed variables between two groups (Zhao, 2004).

Multivariate matching is a method whereby sampling from a large population is done to create a control group (men who did not receive a screening PSA test) of which the distribution of covariates (independent variables) are similar to the distribution of covariates within a treatment group (men who did receive a screening PSA test). Multivariate matching is also a technique used for reducing bias from observed variables in the evaluation of observational studies having numerous possible independent variables (Rubin & Thomas, 1996). Matching with the estimated propensity score (p-score) is a form of multivariate matching defined as the conditional probability that a patient would be assigned to a specific treatment group based on multiple relevant given observed covariates. The resultant p-score is a summary measure that controls for multiple confounders simultaneously by reducing them to a single composite balancing score. This p-score can then be used to match groups thereby reducing selection bias and thus simulating randomization (Rosenbaum & Rubin, 1983). One technique for finding these estimates is by using logistic regression as shown in equation 2, in that

Eq.2 $$\ln \frac{(PS)}{(1-PS)} = \beta_0 + \beta_1 \chi_1 + \beta_2 \chi_2 + \ldots + \beta_p \chi_p$$

and where $$PS = \frac{\exp(\beta_0 + \beta_1 \chi_1 + \ldots + \beta_p \chi_p)}{1 + \exp(\beta_0 + \beta_1 \chi_1 + \ldots \beta_p \chi_p)}$$

is the estimated propensity score found from the logistic model.

Researchers of non-randomized observational studies have no control over those receiving treatment, and covariates are most often not similar (Rosenbaum & Rubin, 1983; Love, 2003; D'Agostino, 1998). Therefore, use of the p-score can adjust for these differences and simulate randomization. However, propensity score matching differs from randomization in that randomized experiments balance the probability distributions on both the observed and unobserved variables between groups, whereas, propensity scores can only balance on the observed variables. Further, the p-score is only an efficient estimator formed from a set of known covariates and makes no statement about the appropriateness of the set. The estimated p-score also does not promise to correct for 100 percent of selection bias or refrain from creating new biases where none exists (Giordano et al., 2008).

Rosenbaum and Rubin (1983) were instrumental in developing the propensity theory during the 1970s and throughout 1980s. Specifically, for the case where treatment equals one (1) and non-treatment equals zero (0), each subject from a sample has only two possible responses, r_1 if the patient received the treatment and r_0 if the patient did not receive the treatment. Rosenbaum and Rubin further suggested that matching using propensity scoring and then stratifying patients by the p-scores into at least five quintiles could eliminate approximately 90% of all the bias (Rosenbaum & Rubin, 1983). Simply put, patients who have the same p-scores but choose different treatments or interventions remain comparable because the distributions of their covariates are balanced.

Propensity scoring has been used in retrospective observational studies where investigators have no control over who receives or does not receive treatment and where large differences in background characteristics exist between groups and should therefore, be controlled (D'Agostino, 1998; Rubin, 1997; Imbens, 2000; Luellen et al., 2005). Because the propensity is a probability, the estimated p-score ranges from 0-1 and will vary depending upon sampling error. For instance, if patients are given an equal (50%) chance of being assigned to either the control group or treatment group (as in the case of randomization) their p-scores would be 0.50 (Luellen et al., 2005). However, in non-randomized observational studies a participant's p-score is a function of their individual characteristics and, therefore would most likely vary from 0.50. For example, if a researcher assigns a 1 as treatment (screening PSA) and a 0 as non-treatment (not screening PSA) then a p-score greater than 0.50 would mean the patient had a higher tendency (propensity) to be assigned to the treatment group and a p-score below 0.5 would mean the patient is less likely to be assigned to the treatment group.

The methods for balancing two groups using propensity scoring analysis were defined by Luellen and colleagues (2005) and Rosenbaum and Rubin (1983) as well as many others. This research study will use matching and stratification. The reason is that this method has been described as being less sensitive than the other methods to nonlinearities in the relationship between p-scores and also because it is easiest and equally efficient as the other methods (Luellen et al., 2005; Rosenbaum & Rubin, 1983; D'Agostino, 1998). The definition of stratification was formally described by Rosenbaum and Rubin in a collection of papers which showed the theorems and provided proofs

developed in 1983 and essentially means that a model can be built to predict the probability that one group would receive a treatment and one group would not where the following notation,

Propensity Score = est. Pr (Treated | background info (covariates))

shows that the propensity score is the estimated probability of being selected to the treatment group based on an individual's background characteristics (observed covariates). Furthermore, it means that groups of subjects having similar p-scores are expected to have similar values of all background information (covariates) within aggregate groups (Love, 2003). Thus stratifying on the p-score produces unbiased estimates of the treatment effect. Since the p-score is a conditional probability of treatment assignment given a set of observed variables, the following expression

$$e(X) = pr(T = 1|X)$$

then defines that treatment assignment T and observed variables X are conditionally independent on the outcome response variable e(X). Therefore, by using a p-score to adjust the estimate of the treatment effect, we can essentially create a quasi-randomized experiment. In other words, if two subjects (one from each group) have the same p-score, then it can be imagined that the two subjects were randomly assigned to each group in the sense of being equally likely to be in the treatment group or control group (Rosenbaum & Rubin, 1983; D'Agostino, 1998; Luellen et al., 2005; Rubin & Thomas, 1996).

Applications of the Propensity Score Method

Studies demonstrating the practical use of the propensity scoring analysis exist in the medical field. These include areas comparing vascular access types and mortality,

education, coronary heart disease and aspirin use, and myocardial infarction as well as others. However, only a few have recently emerged from health services research including areas regarding cancer. In particular, propensity score analysis has been used in studies of screening for breast cancer, chemotherapy and lung cancer, lung biopsies, and long-term survival in men with advanced stage prostate cancer.

In an intense breast cancer screening study, authors assessed the impact on stage of breast cancer at time of diagnosis comparing 58 women who participated in the study from Columbia Presbyterian Medical Center in New York. The 58 women were members of the Women at Risk (WAR) program, a program of research, education, and treatment for women of increased risk for developing breast cancer. The study compared the 58 WAR members to 3,022 non-WAR members listed in the tumor registry and diagnosed from 1991-1997. Interestingly and likened to prostate cancer screening, a crude analysis showed that women in the WAR screening program were diagnosed at significantly earlier stages than non-WAR subjects with a resultant odds ratios of 2.2 and statistical significance with a p value equal to 0.001 (95%CI: 1.37-3.61) (Mitra, Schnabel, Neuget & Heitjan, 2001).

Multiple logistic regression was used to estimate the p-scores for each woman on important relevant covariates. All women were placed into five strata based on the distribution of their respective p-scores. Generally, subjects with very low p-scores were placed in the first quintile meaning that these subjects were less likely to participate in the breast screening program. In contrast, women of the fifth quintile would have the highest p-scores depicting those most likely to participate (Mitra et al., 2001). The results

indicated that before p-score adjustment, 9 out of 16 baseline covariates significantly differed between the two groups thus making matching difficult. These covariates included numbers of pregnancies, numbers of births, age at first delivery, race, how the tumor was discovered, history of prior breast disease, breast cancer in mother, breast cancer in maternal aunt, and breast cancer in sister. There was also a significant difference noted with stage at diagnosis as previously reported in breast screening programs. Comparison between groups after p-score adjustment was accomplished by estimating a two-way analysis of variance (ANOVA) that included the p-score quintile and each of the 16 covariates. Results showed that after adjustment, all 16 covariates were balanced and showed no significant differences. In other words, the two groups were similar within each propensity score quintile. The authors also evaluated screening effect using multiple logistic regression with stage as the outcome variable and WAR membership as the predictor variable with p-scores included as a single variable. Including the p-score as a single variable allowed for a much simpler model than one using all 16 covariates. The final model calculated an odds ratio of 1.52 (95%CI: 0.94-2.46, $p = 0.19$) indicating that although WAR participants were more likely to be staged lower than non-WAR members, the association was not statistically significant (Mitra et al., 2001). The authors concluded that although initial unadjusted analysis suggested that being a member of a screening program was associated with a lower stage disease at diagnosis, statistical significance was lost once adjusting with estimated p-scores thus indicating the importance of considering other factors as reasons for influencing down

staging. The authors noted that using propensity scoring allowed for a more accurate assessment of the effectiveness of an intense screening program in this study.

The effect that chemotherapy had on elderly patients with advanced stage IV lung cancer (non-small cell lung cancer, [NSCLC]) using instrumental variable analysis and the propensity scoring method was also conducted. The authors compared their analysis with the randomized clinical trial results of the Non-Small Cell Lung Cancer Collaborative Group (NSCLCCG) who found that patients treated with chemotherapy had a slight increase in median survival of 6 weeks and a 10% improvement in 1 year survival compared with patients receiving only supportive care (Earle et al., 2001). Using the SEER 11 registry dataset merged to Medicare files, which covered approximately 14% of the U.S. population and a 94% matching rate, the authors were able to show similar results as presented by the RCT listed above. In particular and as seen in the lung RCT, patients more likely to receive chemotherapy were younger, males, non-black race, treated in a teaching hospital, and lived in certain geographic regions. Their results showed that the propensity scores were well balanced with an increased survival of 33 days (42 days in the RCT) and an improvement in 1 year survival of 9% (10% in the RCT). The authors concluded that giving chemotherapy to elderly patients with stage IV lung disease in a non-clinical trial was effective noting slight beneficial results comparable to those seen in the RCT (Earle et al., 2001).

Another study involving lung cancer examined the postsurgical prognosis in patients having non-small cell lung cancer (NSCLC) by comparing those with disease either found by biopsy or found at the time of surgery. Lung biopsy is an important tool

physicians use to help diagnose lung cancer, however, it can sometimes disrupt the vascular and lymphatic structures causing tumor cells to migrate to other areas (Nakajima, Sato & Takamoto, 2005). This may lead to tumor formation in nearby areas or along the biopsy tract and worsen prognosis in patients. Because of the known issues with biopsies the authors used propensity scores to evaluate by comparing prognosis in patients with cancer found at time of surgery to those with cancer found using biopsy. The propensity scores were entered as continuous variables into a Cox proportional hazards model along with other adjusted multiple confounder variables (Nakajima et al., 2005). The results indicated that patients receiving a positive biopsy had a higher risk of cancer recurrence after surgery. Biopsy was shown to be a significant predictor for influencing the recurrence-free rate in patients with NSCLC. It was suggested that the biopsy procedure might worsen the prognosis of patients with resectable NSCLC (Nakajima et al., 2005).

A more recent study compared long-term survival and different treatments in men with advanced stage prostate cancer using propensity scores. The study included 453 men from the Henry Ford Health System between 1980 and 1997 (Tewari et al., 2007). Treatment modalities were compared with two end points using the propensity scoring approach. The end points were overall survival and cancer-specific survival. Patient characteristics indicated that men treated with radiation therapy tended to be older and had more comorbidities than men treated with surgery or watchful waiting. African American men made up nearly 58% of the study population and were less likely to undergo surgery than Caucasians (20% versus 31%). The results showed that for any

given quintile of propensity score men receiving surgery were 68% less likely to die in 10 years than men who chose watchful waiting and nearly 54% less likely to die than men receiving radiation therapy. Propensity scores showed only a slight improvement over the unadjusted rates. The authors noted that using the propensity method was a strength of the study as it allowed the comparison of three treatment modalities when all observed covariates were matched and well balanced (Tewari et al., 2007).

Quality Measures of the Propensity Score Method

Like any statistical analysis, it is important to evaluate the results of tests for quality and accuracy by some criteria before making inferences about relationships and associations. Tools to assess quality of matching can be useful for verifying how well confounders are balanced, especially when provided by graphical illustrations. For example to assess covariate balance, plots of propensity scores for observing overlap and plots of percent absolute standardized differences will be provided.

It is the believed that these examples of visual indicators for covariate assessment and balance will provide useful insight into screening PSA differences as related to each covariate distribution. In addition to graphic illustrations of covariate balance and outcome effects, standard numerical tests for independence for the ordered categorical variables and differences in means for continuous variables on sPSA along with two-sided t-tests, odds ratios, and 95% confidence intervals will be presented.

Data Source

The SEER program is an epidemiologic surveillance system sponsored by the NCI and is comprised of cancer registries throughout various regions across the U.S. The

SEER data is considered highly valid and requires that all registries maintain the highest level of certification for data quality as provided by the North American Association of Central Cancer Registries (Warren, Klabunde, Schrag, Bach, & Riley, 2002). The program's benchmark for completeness of case ascertainment is 98%. The data source for this study is the most recent release of SEER-Medicare linked files from 1986 through 2006. The SEER-Medicare database is a population based cancer registry covering approximately 26% of the U.S. population. The linked data is a collaborative effort of the NCI, SEER registries, and CMS with a greater than 97% matching accuracy rate of SEER individuals to their Medicare claims files (Warren et al., 2002; Wong et al., 2006). The particular SEER dataset used for this study is the SEER 17 registry made up of the following registries: Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, Utah, Los Angeles, San Jose-Monterey, rural Georgia, the Alaska Native Tumor Registry, Greater California, Kentucky, Louisiana, and New Jersey.

The specific files requested from SEER are the Patient Entitlement and Diagnosis Summary File (PEDSF) for men with prostate cancer and the Summarized Denominator Files (SUMDENOM) that includes Part A, Part B, and HMO information, for the period 1986-2006. There is a PEDSF record available for each individual in the SEER database matched to their own Medicare enrollment record. The PEDSF files contain diagnosis information including a patient's date of birth, date of death, sex, race, and state of residence. In addition, there are other variables derived from Census Bureau data on socioeconomic status at the census tract and zip code level. The SUMDENOM files are

generated by the NCI for non-cancer cases. The patients identified from this file represent a 5% random sample of Medicare beneficiaries that live in the SEER areas. These files contain information by calendar year for the months that a person became Medicare eligible from 1986-2006. Each person's file contains their unique Health Insurance Claims number (HIC) with birth date, date of death, sex, race, state of residence, enrollment in both Part A and Part B with a separate file containing socioeconomic information at the zip code level and based on the 1990 and 2000 Census. The HIC number allows for tracking of patients between inpatient and outpatient files and from year to year (Cooper, Yuan, Jethva & Rimm, 2001).

The Medicare files used for this study include the Medicare Provider Analysis and Review (MEDPAR) files for the years of availability (1986-2006). These files contain a single summarized record for each admission and will include up to 10 diagnosis and 5 procedural codes from the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) for the patient as well as all Part A bills for each calendar year. The second linked file requested from Medicare is the Outpatient Claims file for the years available of 1991-2006. This file contains the Part B claims for each calendar year from outpatient providers and ambulatory surgery centers. Information provided through these files include up to 10 diagnostic codes (ICD-9-CM) and 1 procedural code according to Current Procedural Terminology, 4th edition (CPT-4), the HIC number, dates of service, reimbursement amounts, facility provider numbers, revenue center codes and beneficiary demographics. The final file requested from Medicare for this study is the Carrier Claims file also called the physician/supplier or National Claims History record (NCH) and is

available from 1991-2006. This file contains 100 percent of physician/supplier (Part B) bills collected since 1991. These files also contain the HIC number for each patient. Each carrier claim record has a Health Care Procedure Classification Code (HCPCS) describing the billed service. All three of the files requested from Medicare include a 5% random sample of non-cancer cases.

Sample

The unit of analysis for this study includes the SEER regions listed above comprising nearly 26% of the U.S population. The population will include only two races defined as either African American or Caucasian. The ethnic groups of Asian Pacific Islander, Asian-American, and Hispanic/Latino populations are excluded because incidence and death rates were not calculated as a result of the lack of intercensal county population estimates from the U.S. Bureau of Census and because these groups of men have lower incidence and mortality rates than Caucasian men (Edwards et al., 2005; ACS, 2008).

Patient eligibility included elderly men aged 66-85 years who were diagnosed with local/regional prostate cancers (T_1 or T_2) and enrolled in Medicare at least twelve months prior to diagnosis and for at least one month during study period. Although a patient becomes eligible and may enroll in Medicare at age 65, this study will include men beginning at age 66 to ensure at least one year of Medicare claims prior to diagnosis. This will allow more complete data on certain variables, especially comorbid conditions.

Staging is based on the American Joint Commission on Cancer (AJCC) or SEER historic stage code when AJCC staging is missing. Tumor grade is defined as well

differentiated or moderately differentiated using Gleason score notation (Gleason, 1977). Poorly differentiated is excluded because this grade is usually associated with more advanced disease (Gleason, 1977). Search of Medicare files for the appropriate International Classification of Disease, ninth revision (ICD-9) and the Healthcare Common Procedural Coding System codes (HCPCS CPT-4) during 6 months prior to and 6 months after a patient's first PSA test as a Medicare enrollee will identify treatment strategy. The codes for treatment include surgery, external radiation therapy (including brachytherapy implants), neo-adjuvant or adjuvant hormone therapy (ADT), and watchful waiting (see Table 9). A patient receiving external beam after surgery will remain classified as surgical. For example, often men who receive prostatectomy require external beam radiation to protect against possible microscopic disease and to account for positive margins. An assumption is made that all men within the SEER registries of this study will have most likely had PSA tests by the time they reach the age of 66 years. PSA tests will, therefore, be identified from Medicare claims data and categorized according to the theoretical algorithm outlined below. Among men with prostate cancer, two groups (sPSA and dPSA) will be defined as men either having a screening PSA test or men who had PSA tests for any other reason other than for screening purposes (diagnostic reasons). For example, a man will be placed in the treatment group (sPSA) if he had PSA tests for screening purposes or he will be placed in the control group (dPSA) if he had PSA tests for diagnostic reasons and sPSA will be dichotomized as a "Yes" = 1 and dPSA as a "No = 0". The same algorithm and process will be applied to men without prostate cancer to form two similar groups.

Table 9. Patient Eligibility Criteria

SEER site recode	54 (prostate)	
ICD-9 or ICD-10	185.9 or C619	
Medicare enrollment	6 months prior to and after 1st PSA test, men age 66-85 years.	
Men diagnosed with prostate cancer	Localized/regional (SEER defined)	
Staging AJCC/SEER	1 or 2	
Tumor grade	T1: well differentiated (Gleason ≤ 4) T2: moderately differentiated (Gleason 5-7)	1 2
Treatment and CPT code	Surgery Radiation therapy Hormone therapy Watchful waiting	Any form of prostatectomy including partial and radical, CPT 52601, 52612-52614, 55801, 55810, 55812, 55815, 55821, 55831, 55840-55845, 55866 and ICD-9 code 60.5 External beam and brachytherapy implants, CPT 77401-77499, 77416, 77418, 77328, 77778, 77750-77799 and ICD-9 procedural codes 92.21-92.29 and ICD-9 diagnosis codes V58, V66.1, V67.1 and C2638 or C2639, and C2640 or C2641 for brachytherapy stranded or non-stranded I-125 and stranded or non-stranded Pd-103 seeds. HCPCS J9202, J9217-J9219, J1950 and CPT 54520-54522, 54530 and 54535. No treatment CPT-code associated with diagnosis
Screening test	PSA	CPT 84152-84154, and 86316 and screening code G0103
Race	Caucasian African American	

The algorithm to determine whether a man received screening PSA tests or diagnostic PSA tests is illustrated in Figure 4. According to the algorithm, a man will be categorized as having received a PSA test for "screening purposes" if he has no other prostate conditions or prostate treatment related CPT codes listed at the time of his first

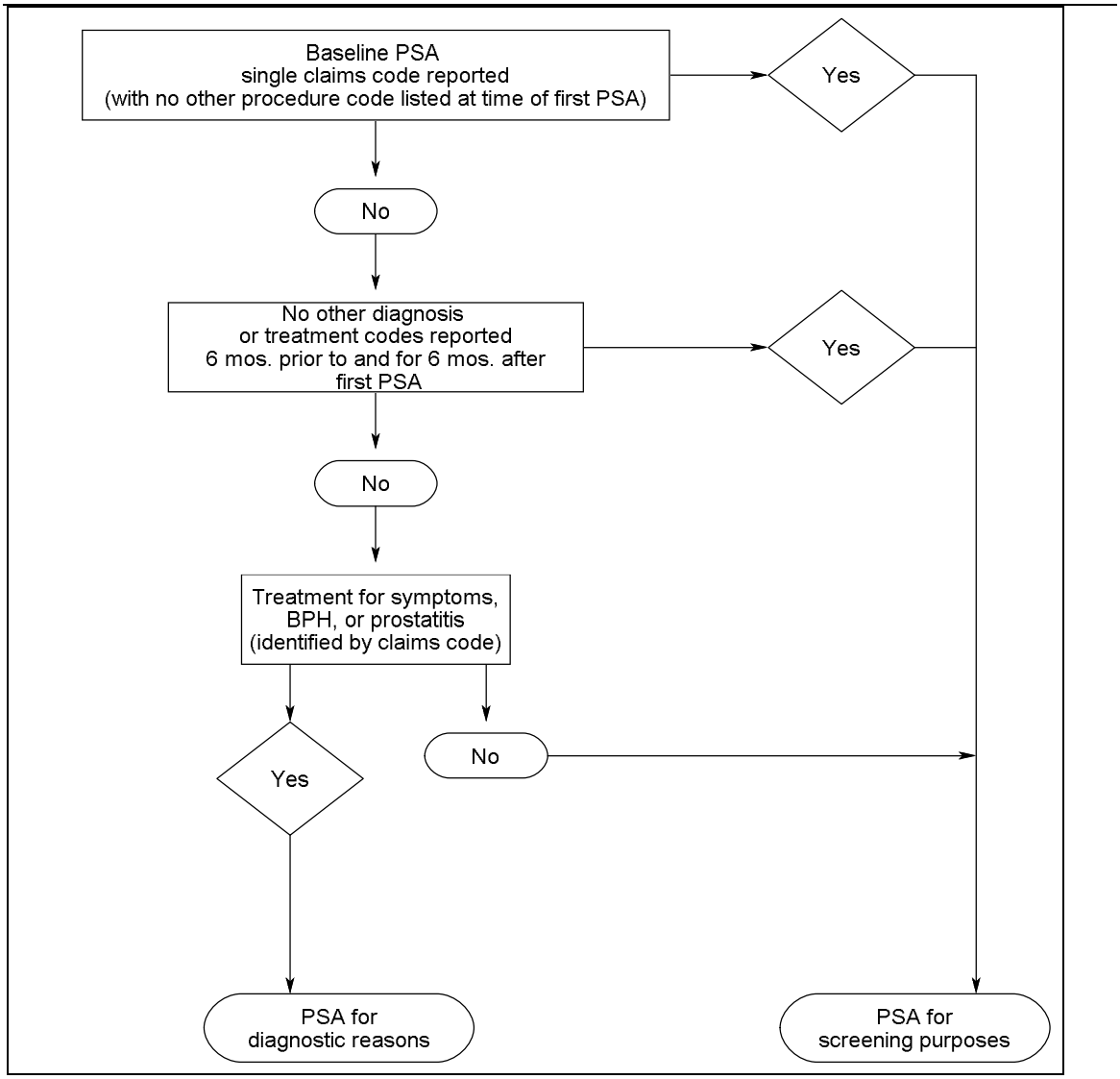

Figure 4. Algorithm to determine screening PSA vs. diagnostic PSA.

recorded PSA test as a Medicare enrollee and for a period 6 months prior to and 6 months after his first PSA test as a Medicare enrollee and/or he was asymptomatic and without any history or treatment for any prostate condition such as BPH or prostatitis (see Figure 4 above). These results will be obtained from the CPT-4 codes listed in the Medicare MEDPAR files, the Carrier Claims files, and/or the Outpatient Claims files. The dichotomized outcome variable of interest is prostate cancer-specific mortality and overall mortality.

Patient exclusion criteria will include those men with previous cancers, a second cancer diagnosed within the same month as prostate cancer, cancer in situ (non-cancerous tumors), less than 66 years old, diagnosis made upon death, neither Caucasian nor African American, no Medicare coverage, and being enrolled within an HMO 3 months prior to diagnosis. Further, men with T_3 or T_4 grade tumors, those with poorly differentiated tumors, and those with metastatic disease will be excluded because this group of men represents those of high grade disease. Men who died of reasons other than prostate cancer (ICD-9 185.9 or ICD-10 C619) will be excluded as well.

Analytic Research Approach

An advantage of the propensity scoring method is that large numbers of covariates can be controlled by multivariate matching and creating a single composite p-score for each quintile thus simplifying the model (D'Agostino, 1998; Rosenbaum & Rubin, 1983; Rubin & Thomas, 1996). For example, adjusting (controlling) for large numbers of variables using traditional model-based regression can lead to large complex and complicated models making diagnostic checks on the goodness of fit difficult to assess.

Also, making interpretations and describing interactions of higher order terms may be difficult as well. The propensity method helps to reduce these difficulties (Mitra et al., 2001).

Rubin and Thomas (1996) showed that values resulting from regression adjustment on unmatched groups can lead to problems of linearity as well (Rubin & Thomas, 1996; Mitra et al., 2001). Therefore to address the question of to what extent PSA screening has on racial disparate mortality rates between African Americans and Caucasians this study will employ a propensity score method as part of its analysis.

Conceptual Model

This study is guided by a treatment and outcomes model outlined by Kane (1997a). Kane (1997b) defined clinical outcomes as the culminated results of many multi-faceted factors. These may include baseline measurements, clinical health status, personal demographic/psychological characteristics, and treatment. In particular, he proposed outlining basic outcomes studies as a function of the factors by the following expression,

> **Outcomes = f (baseline characteristics, personal and clinical characteristics, patient demographic/psychosocial characteristics, treatment [intervention], and p-score).**

This study uses a modified conceptual model in an attempt to isolate relationships between the outcome of mortality and various independent variables with hopes of uncovering the main effect of screening PSA on current racial health disparities (see Figure 5).

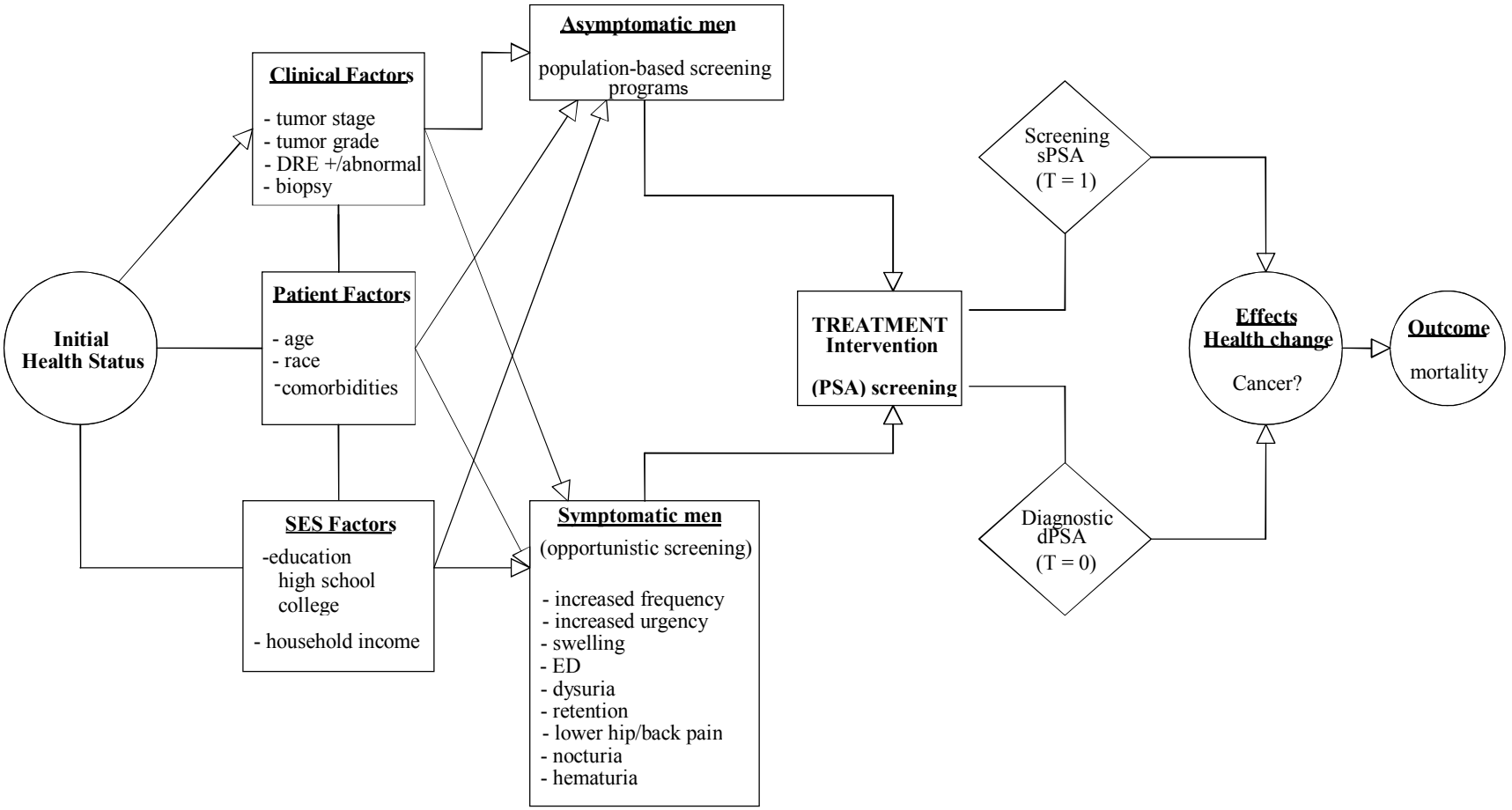

Figure 5. Conceptual Treatment and Outcomes Model.

Research Methodology

This research study is a retrospective, observational exploration of secondary data using the SEER-17 registry dataset linked to Medicare claims registry. The design will consist of a multi-phased process. Baseline characteristics along with summary and descriptive statistics will be determined before matching to note any significant group differences. The same patient characteristics will then be shown to evaluate the accuracy of the matching process. Table 10 is a simple illustration that quickly shows the difference in groups before and after matching and serves as a sample of how the data may look for this study.

All independent variables were selected as previously identified in the review of the literature and defined based on the student's knowledge. In the next step, a propensity logistic regression model will be developed to estimate p-scores using the treatment (sPSA) as the dependent variable. Secondly, men will be matched based on having comparable p-scores and placed into one of five quintiles, where the first quintile indicates a lower propensity to screen (near 0) and the fifth quintile a greater propensity to screen (near one). The covariate distribution can then be examined using quality assessment tools previously described and by noting effects when using adjusted p-values. The propensity logistic regression model will yield estimates of the probability distribution to receive the intervention (sPSA) and will range from 0-1. Through this step, p-scores are created by saving the predicted probabilities from the logistic model. This is an informative step to eliminate differences in the two groups and is not a formal hypothesis test. The covariates chosen will be included in a final main effects logistic

Table 9. Sample Baseline Characteristics by Group with Resultant p-scores before and after matching.

Before matching on p-score			
Variable	sPSA (%)	dPSA (%)	P value
Age	72	66	P < 0.05
AA	34	57	P < 0.05
Caucasian	73	35	P < 0.05
Stage			
T1	74	45	P < 0.05
T2	66	38	P < 0.05
Grade			
1	62	28	P < 0.05
2	55	33	P < 0.05
After matching on p-score			
Variable	sPSA (%)	dPSA (%)	P value
Age	71	70	P = 0.33
AA	44	47	P = 0.23
Caucasian	55	57	P = 0.46
Stage			
T1	62	59	P = 0.37
T2	54	55	P = 0.78
Grade			
1	53	49	P = 0.47
2	45	44	P = 0.79

regression model and listed in table format (see example Table 11). From this output table, the odds ratios for each variable can be calculated as e^b. And the z statistic is the ratio of the regression coefficient (ß) to the standard error SE(ß). Also 95% confidence intervals may be determined for each variable. Assessment of whether the p-score adjustments help to balance the covariates is illustrated by graphical display with adjusted p-values where in this case, p-values > 0.05 would indicate no significant differences

Table 10. Sample Main Effects Logistic Regression Model.

Predictor Variable	Regression Coefficient ß	Standard error SE(ß)	WALD (chi^2)	Sig. p-value	95% C.I.
Intercept (constant)					
Variable (x_1)					
Variable (x_2)					
Variable (x_3)					

between covariates and, therefore balance being achieved. In reviewing the propensity model results, interest is in the coefficients of the sPSA variable for non-statistically significance ($p > 0.05$) indicating balance. If balance is achieved on all covariates within each strata, meaning there are no differences in the two groups, then it is safe to assume that most selection bias has been removed and a quasi-randomized study design achieved. Results of the first model with calculated p-score adjustments will be provided by subsequent logistic and Cox regression modeling.

Assessment of covariate distributions within each quintile may show the inability to detect differences after p-score adjustment. For example, the initial regression model should indicate sufficient overlap of covariates by showing no extensive or consistent patterns of interactions between screening PSA and each quintile. This would allow for p-score adjustments in all subsequent regression models to explicitly account for selection bias. Should assessment of overlap prove sufficient, subsequent logistic and Cox models can be used for the final group comparison. The five quintiles will be displayed (see

Table 12) according to their p-scores with mathematic absolute percent differences in p-scores for the outcome variables. Finally, logistic regression and Cox regression models of main treatment effects (sPSA) on mortality between races will be developed and formal hypothesis testing performed.

Table 11. Summary of Propensity Scores, Count, and Means for Race.

Strata	Counts, n (%)		Means		Standardized Absolute Difference
Propensity Score	sPSA	dPSA	Cancer	Non-cancer	
Quintile 1					
Quintile 2					
Quintile 3					
Quintile 4					
Quintile 5					

Study Variables

The study variables are provided later in the section for the independent variables and the dependent variable. Age will be categorized into groups ranging from 66 to over 85 years. Race is categorized as either Caucasian (1) or African American (2) according to SEER race recode in the PEDSF file. Tumor stage will be ordered as either T_1 (1) or T_2 (2). Tumor Grade will be categorized as I or II. Socioeconomic factors will be determined from SEER data and because SEER-Medicare does not collect individual level socioeconomic status, this study will use Census Tract 2000 by percent mean for non-high school graduate, high school graduate, some college (no degree), four years of

college (degree), and mean median household income as proxies for an individual's socioeconomic status.

Summary comorbidity measures will be assessed using a modified Charlson index known as the NCI combined indices described by Klabunde et al., 2000 and 2007. The NCI combined measure, unlike the Charlson indices which include using data from only one source (inpatient files), builds on the Charlson index by not only using inpatient claims but also physician claims data. It was shown that by using the two sources, better fit models resulted (Klabunde, Potosky, Legler & Warren, 2000; Klabunde, Legler, Warren, Baldwin & Schrag, 2007). The NCI combined approach derives weights calculated from conditions identified from either the inpatient or physician claims files and combines them into a single index. This method has demonstrated improved prediction of non-cancer mortality and treatment choice for breast and prostate patients (Klabunde et al., 2000; Klabunde et al., 2007). Their study used SEER-Medicare files that identified 53,503 eligible Medicare beneficiaries with prostate cancer. The authors found estimated hazard ratios or coefficients from survival estimation models, multiplied these weights by a dichotomized condition indicator (1 = having the condition and 0 = not having the condition) and then summed the weighted conditions to construct the single index. The weighted estimate values have been empirically derived and published values for the twelve most prevalent conditions will serve as the basis for the comorbid indices of this study. For clarification purposes, the comorbid conditions old myocardial infarct and myocardial infarct are described by ICD-9 diagnostic codes as men who have had a prior heart attack that has healed and exhibit no current symptoms or an acute heart

attack within the last 8 weeks, respectively. The outcome variable (dependent variable) used for this research study will be prostate cancer-specific mortality and overall mortality as recorded on death certificates within SEER files and as listed as cause of death where "Yes" = 1 or "No" = 0 (see Table 13).

Table 12. Study Variables.

Independent variables	
Name	**Type**
Age Groups at diagnosis (yrs.)	Categorical
66-69 referent variable	14
70-74	15
75-79	16
80-84	17
Race	Categorical
Caucasian	1
African American	2
Stage	Binary
Local/Regional	1
In situ + Localized + Regional	0
Grade	Categorical
Grade I (Gleason ≤ 4)	1
Grade II (Gleason 5-7)	2
Screening PSA	Binary
Yes	1
No	0
Treatment	Categorical
Radiation	1
Radioactive implant	2
Any surgery	3
Hormone therapy	4
Socioeconomic Status (SES) Variables	
Marital Status	Nominal
Single/never married	1
Married	2
Separated	3
Divorced	4
Widowed	5
Unknown	9

Table 13: continued.

Census Tract Education	Continuous
≤ 12 years (non-high school grad)	% mean
≥ 12 years (high school grad)	% mean
College Education	Continuous
Some college (no degree)	% mean
At least 4 years of college	% mean
Census Tract Median Household Income (USD)	Continuous
By zip code (% mean)	% mean
Comorbidity Indices (NCI- combined)	Continuous
Previous Myocardial Infarct	Coefficient
Myocardial Infarct	0.054
Congestive Heart Failure	0.242
Peripheral vascular disease	0.874
Cerebrovascular disease	0.359
COPD	0.266
Dementia	0.725
Paralysis	0.777
Diabetes	0.393
Diabetes with sequelae	0.239
Chronic Renal Failure	0.440
Rheumatologic disease	0.678
	0.021
Dependent variable	
Overall Mortality	Binary
Yes	1
No	0
Prostate Cancer-Specific Mortality	Binary
Yes	1
No	0

Hypothesis Testing

All statistical testing will be set to an $\alpha = 0.05$ and two-sided. Summary and descriptive statistics using tests of proportions for all categorical independent variables and tests for differences in means for all continuous independent variables, including an ANOVA for the SES variables among the non-cancer group will be provided.

To test the hypothesis H_1 that no statistically significant differences exist in prostate cancer-specific mortality rates among race for men with PSA screen detected cancer and men with clinically diagnosed cancer, cancer-specific mortality will be calculated and tests of proportions using logistic regression with odds ratios, confidence intervals, and p values compared. In addition, a sensitive analysis using conditional Cox regression models for censoring on time to event and to account for matched pairings will be evaluated to compare results with other models. In testing the hypothesis H_2 that no statistically significant differences exist in overall mortality rates among race for men without prostate cancer receiving screening PSA tests and men receiving diagnostic PSA tests, overall mortality will be calculated with tests of proportions using logistic regression and odds ratios, confidence intervals, and p values reported for comparison; conditional Cox regression models will be applied as a means of comparison with the results of other models as well.

To test hypothesis H_3 that baseline (initial) PSA utilization rates among race in men with prostate cancer during the PSA era from 1986-2006 will show no statistically significant differences, F-Tests with one-tailed probability distributions will be reported. Likewise, to test hypothesis H_4 that baseline (initial) PSA utilization rates do not differ among men without prostate cancer during the PSA era, F-Tests with one-tailed probability distributions will be calculated for the same time period. The PSA utilization rates for testing H_4 will be derived from the SUMDENOM file of a 5% randomized group of men without prostate cancer.

Study limitations

Medicare Data Limitations

A limitation of the Medicare files is that not all services provided are captured in the claims files. For example, PSA screening provided by a community based screening program, services provided to a beneficiary by a Veteran's Administration facility, or services to a beneficiary who is employed and currently covered by a health plan (where Medicare would be the secondary payor). Other non-covered services are long-term care and lack of Hospital Maintenance Organization (HMO) enrollment (Warren et al., 2002). For example, HMOs are not required to send claims data on their enrollees to Medicare. This is a problem because HMO enrollees made up about 14% of the Medicare population as of 2001 with proportions varying greatly across SEER regions. For instance, some states have very little HMO enrollees while other states have high concentrations of HMO participants. Further, enrollees are free to move from one HMO to another and HMOs can sign up new participants anytime thus potentially increasing the number of missing data during a particular year. Because Medicare does not contain complete data on enrollees within HMOs, men that were enrolled into an HMO 3 months prior to diagnosis are excluded.

It is also known that using claims data to estimate prostate screening is limited (Freeman et al., 2002; Potosky et al., 1995; Legler et al., 1998; Cooper et al., 2001). For instance, claims data may lead to incomplete or missing information, as they are sometimes created only for purposes of payment and therefore reasons for having PSA tests (screening vs. diagnostic) are not provided. However, with the expansion of

Medicare's coverage and using the latest SEER-Medicare data coupled with use of the proposed algorithm in Figure 4, it is hopeful that distinguishing screening PSA tests from diagnostic PSA tests will be more accurate.

SEER Data Limitations

Generalization of the SEER data files to the U.S. population of elderly may be limited. The SEER registries were not randomly selected instead they were chosen based on quality of data submission and to adequately represent minority groups. Also, determining SES variables at the individual level is not possible within the SEER files therefore, only proxy measures using census tract data will be used. In order to investigate comparisons of SEER registrants to the national U.S. population, the NCI examined SES characteristics, HMO enrollment, and cancer mortality.

In looking at SES factors of age groups and sex, NCI found persons within the SEER areas to be comparable to the elderly within the U.S. population (Warren et al., 2002). However, with race they found differences. According to the 1990 census, the SEER areas tended to have lower proportions of Caucasians and higher proportions of other races. Also, individuals within SEER regions were more likely than persons within the U.S. population to live in urban areas (87% vs. 73% respectively) and more likely to live in affluent areas with only 9.5% of SEER individuals living in households with incomes below the poverty level compared with the U.S. average of 12.8% (Warren et al., 2002). Regarding the lack of HMO data, the same problem exists for the SEER files as in the Medicare files in that the proportion of SEER registrants enrolled in HMOs was

considerably greater than the U.S. populations with variations across states that could lead to greater numbers of missing data as well.

Racial differences in mortality for men with prostate cancer have been previously noted with the NCI also noting that differences exist among SEER areas and the U.S. total. For all races, cancer mortality rates among men living in SEER areas compared to the U.S. total population were approximately 4% lower (218 versus 226.4 per 100,000 men). When comparing race among men living within SEER areas and the U.S. total, African Americans had an approximate 2 times greater mortality rate than did Caucasians (417.7 versus 210.6). These values are consistent with chapter one's mention of the American Cancer Society's more recent numbers showing that African Americans were 2.4 times more likely to die from prostate cancer than Caucasians (ACS, 2008; ACS-AA, 2008; Warren et al., 2002).

Because of misclassification bias or inaccurate cause of death listed on death certificates, SEER data calculates mortality based on incidence data. This incidence-based mortality (IBM), examines mortality rates by variables determined at time of diagnosis, such as stage. Only the SEER files provide cause of death derived by the IBM method, therefore it will be used for determining prostate cancer-specific mortality within this study.

Further, large administrative databases contain large amounts of selection bias threatening validity when using observational data for estimating outcomes. Attempting to control for this bias can be achieved by using multivariate matching such as propensity scoring analysis. However, it is suggested that it may be impossible to remove all

selection bias with any statistical analysis (Giordano et al., 2008). Potential explanations for selection bias that remains even after controlling is lack of information for unobserved and unmeasured covariates as well as lack of information on self-reported health surveys.

CHAPTER 4: RESULTS

Introduction

As presented in Chapter 3, this research study is a retrospective, observational exploration of secondary data using the SEER-17 registry dataset linked to the Medicare claims registry. It provides an analysis of the association between prostate cancer screening with PSA testing and the effects of such tests on racial disparate mortality between African Americans and Caucasians. The study utilizes a fairly new method in the propensity analysis applied to both logistic regression and conditional Cox regression modeling.

First, results for the prostate cancer cases are presented beginning with a traditional logistic and Cox regression model for the full unmatched data set without use of a propensity analysis. These models are compared to both the logistic and conditional Cox regression models that do have a propensity analysis later in the chapter. Subsequent results from the logistic and conditional Cox regression models with a propensity analysis applied are presented in a multi-phase approach with responses to research questions one and three and hypothesis H_1 and H_3 provided in Chapter 5 Discussion. The multi-phase approach begins with (a) sample selection, (b) demographics and data characteristics, (c) group selection, (d) propensity analysis, (e) propensity logistical and conditional Cox regression models (Luo, Gardiner, & Bradley, 2009), and (f) final comparisons of

propensity matched regression models to traditional non-propensity regression models. The same systematic approach was repeated for the non-cancer group for examining research questions two and four and hypotheses H_2 and H_4. However, although the analysis for the non-cancer group will include the same detailed steps as noted above for the prostate cancer group, the reported results include less descriptive detail within items (a), (b), and (c) above and only select detailed results for (d), (e), and (f) above.

The Prostate Cancer Analysis

Sample Selection

The selected sample originated from the linked SEER-Medicare registry consisting of one file from SEER (PEDSF) and 3 files from Medicare (MEDPAR, NCH, and Outpatient claims). The data make up almost 26% of the U.S. population with over 224 million individual claims within 235 files searched. A total of 515,802 prostate cases registered through the study period before exclusions were identified. Table 14 shows the final exclusion criteria for all races that resulted in omitting 443,025 men and leaving a selected sample size of 72,777 men. There are statistically significant differences in the distribution of causes of exclusions between Caucasians and African American men; however, the largest variance occurred with having more African Americans being younger than 66 when diagnosed with prostate cancer. Further, African Americans were slightly more likely to be diagnosed with a greater degree of poorly differentiated tumors and approximately 20% less likely to have early stage disease compared with Caucasians. From this selected sample of all races, final exclusion criteria by race resulted in retaining

Table 13. Exclusion Criteria for Selected Sample.

Exclusion Criteria	Freq.	%	Cum. Freq.	Cum. %
Diagnosed before year 1987	16,356	3.17	16,356	3.17
Race not Caucasian or AA	63,884	12.39	80,240	15.56
First cancer is not prostate	25,124	4.87	105,364	20.43
Age group at diagnosis <65y or unknown	92,462	17.93	197,826	38.35
Age at diagnosis <66	17,158	3.33	214,984	41.68
Poorly differentiated tumors	107,513	20.84	322,497	62.52
Not local/regional disease	64,130	12.43	386,627	74.96
Another cancer diagnosed in same month	1,532	0.30	388,159	75.26
Died of reasons other than prostate cancer	26,088	5.06	414,247	80.31
Diagnosed from death certificate only	2	0.00	414,249	80.31
Unknown month of diagnosis	290	0.06	414,539	80.37
HMO within 3 months before diagnosis	22,248	4.31	436,787	84.68
Not in both Part A & B within 3 months before diagnosis	6,238	1.21	443,025	85.89
Final Selected Sample	**72,777**	**14.11%**	**515,802**	**100%**

65,738 (90.3%) Caucasians and 7,039 (9.3%) African Americans ($\chi 2$ 3225.43, df 12, $p<0.0001$). A majority of exclusions for race included men with poorly differentiated tumors (93,471), diagnosed before reaching 65 years of age (76,721), and men diagnosed with greater disease extent than local/regional tumors (see Table 15). A smaller proportion were excluded for race because of death from something other than having prostate cancer (22,899), first cancer diagnosis not prostate cancer (22,713), and being a member in an HMO at least three months prior to diagnosis (19,819). Even fewer men were excluded for other various reasons such as not being a member in both part A and B of Medicare, other cancers diagnosed, and finally the month of diagnosis was unknown.

Table 14. Exclusion Criteria of Selected Sample by Race.

				Percentage of exclusions		
Exclusion Criteria	**Cauc.**	**AA**		**Cauc.**	**AA**	
			Total			Total
Diagnosed before year 1987	14,093	1,367	15,460	3.55	2.42	3.43
first cancer is not prostate	22,713	2,411	25,124	5.76	4.26	5.57
age group at diagnosis <65y or unknown	76,721	15,741	92,462	19.45	27.82	20.50
age at diagnosis <66	14,625	2,533	17,158	3.71	4.48	3.80
poorly differentiated tumors	93,471	14,042	107,513	23.70	24.81	23.84
not local/regional	57,550	6,580	64,130	14.59	11.63	14.22
another cancer diagnosed in same month	1,369	163	1,532	0.35	0.29	0.34
died of reasons other than prostate cancer	22,899	3,189	26,088	5.81	5.64	5.78
Diagnosed from death certificate only	0	2	2	0.00	0.00	0.00
Unknown month of diagnosis	256	34	290	0.06	0.06	0.06
HMO within 3 months before diagnosis	19,819	2,429	22,248	5.02	4.29	4.93
not in both Part A & B within 3 months before diagnosis	5,179	1,059	6,238	1.31	1.87	1.38
Selected Sample	65,738	7,039	72,777	16.67	12.44	16.14
Total	**394,433**	**56,589**	**451,022**	**100%**	**100%**	**100%**

Demographics and Data Characteristics

Independent variables by race of the population sample show that significant statistical differences exist for the variable age among race ($\chi 2$ 198.84, df 4, $p< 0.0001$); however, no differences were noted for the mean age at which a man was diagnosed (73years for Caucasians and 72 years for African Americans). Further, it is noted that based on percentage, more African American men were likely to be in the younger age

group (66-69 years) with the remaining age categories relatively equal. Significant differences were also noted for the variable historic stage ($\chi 2$ 28.24, df 4, $p < 0.0001$) with most cases being staged as localized/regional for both races according to SEER definition (95.7% and 96.7%). For these reasons, the variable historic stage was combined and recoded as binary where a value of "1" was assigned as local/regional and a value of "0" assigned as all other categories. Only slight differences among race were noted for grade (χ^2 4.757, df 1, $p = 0.029$) with a majority of men in both races having grade II defined as having Gleason scores ranging from 5-7 (93% of total); however, significant differences were seen for the categorical variable marital status (χ^2 1575, df 5, $p < 0.0001$) where 73% of the total population were married. Within the marital status variable, African American men were more likely to be single/ never married and less likely to be married. Finally, for the remaining marital status categories, African American men were more likely to be separated, divorced, and/or widowed than Caucasian men in this selected sample (see Table 16).

Socioeconomic status by race and zip code is depicted according to Census Tract 2000 data. There are significant statistical census differences seen in the distribution throughout all the variables ($p < 0.0001$). Specifically, the mean percent of African Americans having less than a high school education is nearly twice that of Caucasians whereas almost the opposite is seen when comparing Caucasians to African Americans having four years of college. Income disparities among race also indicate the mean median income shows that, on average, Caucasians earned nearly 1.5 times more than

Table 15. Summary Count and Percentage for Variable by Race.

Race	Caucasian	African
	n (%)	n (%)
Age Group (yrs.)		
66-69	19,898 (30.3)	2,654 (37.7)
70-74	23,112 (35.2)	2,393 (34)
75-79	15,187 (23)	1,389 (19.7)
80-84	5,864 (8.9)	447 (6.4)
85+	1,677 (2.6)	156 (2.2)
Mean age at diagnosis	**73 yrs.**	**72 yrs.**
Historic Stage		
0 (in situ)	6 (0.01)	1 (0.01)
1 (localized)	2,780 (4.2)	217 (3.1)
2 (regional)	38 (0.06)	10 (0.14)
8 (localized/regional)	62,893 (95.7)	6,808 (96.7)
9 (unstaged)	21 (0.03)	3 (0.04)
Grade		
I (Gleason <5)	4,378 (6.7)	421 (6)
II (Gleason 6-7)	61,360 (93.3)	6,618 (94)
Marital Status		
1 (single, never married)	3,657 (5.6)	940 (13.4)
2 (married)	48,957 (74.5)	4,073 (57.9)
3 (separated)	178 (0.27)	108 (1.5)
4 (divorced)	2,357 (3.6)	607 (8.6)
5 (widowed)	4,778 (7.3)	712 (10.1)
9 (unknown)	5,811 (8.73)	599 (8.5)
Total	**65,738 (90.3)**	**7,039 (9.7)**

African Americans during the study period. Regarding whether a man completed high school or had some college, no differences were noted between races (see Table 17).

Counts and percentages for the variables of treatment by race illustrate that for radiation treatments, African Americans were only slightly more likely to receive external beam radiation than Caucasians. Regarding radioactive implants, Caucasians were only somewhat more likely to have a prostate seed implant than African American

Table 16. Socioeconomic Status by Race (Percent by zip code Census Tract 2000).

	Caucasian						African American							
Percent by zip code (Census Tract 2000)	**N**	**N non missing**	**Mean**	**Std. Dev.**	**Min**	**Max**	**N**	**N non missing**	**Mean**	**Std. Dev.**	**Min**	**Max**	**N Total**	**p-value**
	65,738						**7,039**						**72,777**	**of t-tests**
Non High School Graduate		63,128	15.30	10	0	100		6,763	27	12	1.81	75		**<.0001**
High School only		63,128	26	10	0	80		6,763	28	7	5	50		**<.0001**
Some College Education		63,128	28.66	7	0	100		6,763	26	6	7.78	53		**<.0001**
College Education (4 years)		63,128	30.05	17	0	94		6,763	18	12	0	78		**<.0001**
Median Income		63,128	$53,826	$21,816	$7	$200,008		6,763	$36,961	$14,739	$7	$146,762		**<.0001**

men. The remaining treatment levels of radiation are more closely balanced based on percentages; however, significant differences do remain ($\chi 2$ 194, df 9, $p<0.0001$).

The SEER registry changed the name of its variable for defining surgery of the prostate during this study period. The first name used, Site Specific Surgery, covered the period 1983-1997 and the second, Surgery of Primary Site, covered from 1998 onward. For the variable name Site Specific Surgery, prior to 1998 a majority of the sample population (82.5% Caucasians and 84% African Americans) either had no surgery or had surgery after 1998, and would therefore, be categorized by the new variable name Surgery of Primary Site. Only a small portion of men had needle biopsies (7.7% Caucasians and 8% African Americans), transurethral resection of prostate (TURP) combined with a surgical process that freezes the prostate called Cryoprostatectomy (2.2% Caucasians and 3.5% African Americans) or radical prostatectomy with or without lymph node dissection (4.8% Caucasians and 2.4% African Americans). The remaining surgical types performed prior to 1998 were negligibly small ($\chi 2$ 138, df 17, $P < 0.0001$). The new surgery variable name Surgery of Primary Site began during 1998 and illustrates that 84% of Caucasians and 85.2% of African American men either had surgery recorded under the previous surgical period or had no cancer-directed surgery at all. A small number of men had a TURP with either an incidental benign cancer finding or with a positive cancer finding. And only a slightly larger portion of both races chose to have a radical prostatectomy surgery ($\chi 2$ 91, df 16, $p < 0.0001$). Again, because the percentage of men having no surgery was high compared to that of men having any of the other surgical choices combined, the two variables, Site Specific Surgery and Surgery of

Primary Site were combined and recoded as binary where a value of 1 was assigned as a "yes", a man had some type of prostate surgery during the study period and a value of 0 assigned as a "no", a man had no surgery of any type during the study period.

In reviewing the variable radiation sequence with surgery, it is noted that of the total sample population, 97% of Caucasians and 96% of African Americans had no radiation and/or surgery. Only a small sample of men had external radiation after surgery which is a common treatment sequence when managing patients who have chosen prostatectomy followed by external beam radiation (χ^2 36, df 6, $p < 0.0001$). Because the percentage of men from both races receiving no sequence of radiation with surgery was vastly different from the percentage who did and because the sample population for this study is sufficiently large, the variable radiation sequence with surgery was combined and recoded as binary with a value of "1" assigned as "yes", a man had some sequence of radiation and surgery and a value of "0" assigned as "no", a man had no combination of radiation with surgery.

Regarding whether men received hormone therapy, a majority among both races elected not to have hormones at the time of their diagnosis (93% Caucasians and 88% African Americans). In addition, if race were independent of receiving hormone therapy at the diagnosis date, the data show that 99% of men could be expected **not** to receive hormone therapy (χ^2 34, df 1, $p < 0.0001$). However, Caucasians were almost twice as likely as African Americans not to take hormone therapy within this population sample (OR 1.941, 95%CI 1.55-2.431).

In contrast, the decision not to have hormones decreased by almost one half during the 6 months following a diagnosis date (43.7% Caucasians and 44.6% African Americans). The test for independence between race and hormone therapy up to 6 months after being diagnosed shows that only 86% of men could be expected not to have hormones (χ^2 36, df 1, $p < 0.0001$). Further, Caucasians remained only slightly more likely **not** to receive hormones than African Americans at the 6 month time (OR 1.32, 95%CI 1.208-1.452) (see table 18).

Group Selection

The two groups, screening PSA and diagnostic PSA, were selected according to the algorithm in Figure 4 above. A man was considered as having a true screening PSA (sPSA) if during the period 6 months prior to and 6 months after receiving his first PSA test as a Medicare enrollee the test was not associated with any other prostate condition, treatment, or symptom. Other conditions for being placed in the dPSA group include prostate surgery, histologic malignancy diagnosis, bladder neck obstruction, unspecified urinary tract infection, hematuria, increased frequency or abnormality in urination, radiation, or hormones. If any of these conditions or diagnoses were identified by claims codes CPT-4 or ICD-9, men were placed in the diagnostic group (dPSA); otherwise, they were placed in the screening group (sPSA). The number of men in the sPSA is slightly less than the number in the dPSA at 32,210 and 37,854 (final n = 70,064). When comparing race, there are statistically significant differences in the likelihood that Caucasian men received a sPSA test compared with African American men (χ2 291.5, df 1, $p<0.0001$). Specifically, Caucasians were 1.6 times more likely to have a sPSA than

Table 17. Summary Count and Percentage for Treatment by Race.

Treatment		SEER Race Recode B	
		Caucasian	African American
		n (%)	n (%)
Radiation	None	32,526 (49.5)	3,424 (48.6)
	Radiation Beam	17,420 (26.5)	2,164 (30.7)
	Radioactive Implants	9,026 (13.7)	624 (8.9)
	Combination Radiation beam/implants	4,409 (6.7)	562 (8.0)
	Recommended, unknown if administered	726 (1.1)	103 (1.5)
	Unknown	796 (1.2)	60 (0.9)
Radiation sequence with surgery	No radiation and/or cancer-directed surgery	63,798 (97)	6,753 (95.9)
	Radiation after surgery	1,734 (2.6)	259 (3.7)
Site Specific Surgery	Men part of next sequence SXPRIM1 (1998+)	54,219 (82.5)	5,914 (84)
	No surgical procedure	485 (0.7)	59 (0.8)
	Incisional, needle, or aspiration biopsy of primary site	5,048 (7.7)	562 (8.0)
	Unknown if surgery performed	163 (0.2)	9 (0.1)
	TURP, Cryoprostatectomy w/o lymph node dissection	1,463 (2.2)	173 (3.5)
	Radical Prostatectomy w/o lymph node dissection	779 (1.2)	101 (1.4)
	Radical Prostatectomy with lymph node dissection	3,172 (4.8)	166 (2.4)
Surgery of Primary Site (1998+)	Men part of previous sequence SSSurg (1983-1997)	30,179 (45.9)	3,238 (46)
	No cancer-directed surgery	25,129 (38.2)	2,756 (39.2)

Table 18: continued.

Treatment		SEER Race Recode B	
		Caucasian n(%)	African American n(%)
Surgery of Primary Site (1998+) continued	TURP, NOS	288 (0.4)	52 (0.7)
	TURP, cancer incidental finding during surgery; benign	1,917 (2.9)	167 (2.4)
	TURP with cancer finding	651 (1.0)	127 (1.8)
	Cryoprostatectomy	195 (0.3)	31 (0.4)
	Radical Prostatectomy	6,671 (10.1)	604 (8.6)
	Unknown	478 (0.7)	35 (0.5)
Hormones at time of diagnosis	No	61,285 (93.2)	6,179 (87.8)
	Yes	470 (0.7)	92 (1.4)
Hormones 1-6 months after	No	28,068 (43.7)	3,142 (44.6)
	Yes	4,222 (6.4)	626 (8.9)

African Americans (OR 1.585, 95%CI 1.503-1.671). Among African Americans, a much lower percentage were screened compared to those having diagnostic PSA tests; only 33% received sPSA tests while 59% received dPSA tests. The variance illustrates that African American men were more likely to have their prostate cancers clinically diagnosed by waiting until they become symptomatic before seeing a physician instead of using early detection screening tests. These values coincide with the literature which shows that African American men historically only visit their physician when symptoms occur, resulting in use of the PSA test for screening purposes 10% less frequent than Caucasians (Behavioral Risk Surveillance System, Public Use Data File, 2004).

Although this study does not include men who never had a PSA test recorded in any of their claims files, it is worth noting that 2,713 or almost 4% of the selected sample population met that definition. In addition, there is a significant difference in the likelihood that African Americans would even have a PSA test (χ^2 467.5, df 1, $p < 0.0001$) and they are only 36.6% as likely to have a PSA at all compared to Caucasians (OR 0.366, 95%CI 0.333-0.402) (see Table 19).

Table 18. Summary Count and Percentage for Study Group by Race.

SEER RACE	**Group**			
	Screening PSA n (%)	**Diagnostic PSA n (%)**	**No PSA n (%)**	**Total n (%)**
Caucasian	29,896 (45.5)	33,718 (51.3)	2,124 (3.2)	65,738 (100)
AA	2,314 (33)	4,136 (59)	589 (8)	7,039 (100)
Total count	32,210 (44.3)	37,854 (52)	2,713 (3.7)	72,777 (100)

Characteristics of the independent variables for the two study groups are shown in Table 20 and demonstrate differences among sPSA and dPSA groups. For the variable age, the greatest variance is shown among younger men within the age category from 66 to 69 years old with almost twice as many having dPSA tests as having sPSA tests (χ^2 974, df 1, $p < 0.0001$). This may be explained by less men of this age range participating in community screenings or perhaps these younger men are not visiting a physician until they become symptomatic. The remaining levels within age were somewhat more balanced.

Table 19. Summary Count and Percentage for Study Groups by Independent Variable.

Group by Independent Variables		**Screening PSA**	**Diagnostic PSA**
		n (%)	n (%)
SEER Race Recode B	Caucasian	29,896 (47)	33,718 (53)
	African American	2,314 (36)	4,136 (63)
Age Group at Diagnosis Year	66-69	7,994 (37)	13,444 (63)
	70-74	12,182 (49)	12,433 (51)
	75-79	8,249 (51)	7,855 (49)
	80-84	3,004 (49)	3,143 (51)
	85+	781 (44)	979 (56)
Historic Stage	In situ	158 (6)	2,514 (94)
	Localized	5 (71)	2 (29)
	Regional	24 (51)	23 (49)
	Localized/Regional	32,012 (48)	35,303 (52)
	Unstaged	11 (48)	12 (52)
Grade	I (Gleason score ≤ 4)	1,861 (41)	2,688 (59)
	II (Gleason score 5-7)	30,349 (46)	35,166 (54)
Marital Status	Single, never married	1,830 (41)	2,582 (59)
	Married	23,937 (47)	27,323 (53)
	Separated	97 (38)	157 (62)
	Divorced	1,098 (42)	1,533 (58)
	Widowed	2,369 (45)	2,862 (55)
	Unknown	2,879 (46)	3,397 (54)

Previous definitions used by SEER for the individual stages of localized and regional tumors included those confined to the organ of interest and which had not yet extended beyond the outer membrane directly into surrounding organs or into the lymphatic system. In addition, SEER included all in-situ staged prostate cancers as non-invasive tumors and that had also not yet penetrated the gland's peripheral membrane or extended outside the membrane. Further, prior to 1994 prostate cancer cases were not coded using a stage variable at all; however, during the year 1994-1995 SEER made a change to the older variable historic stage and began using a combined variable for all local and regionally staged prostate cancer cases. The combined variable is called local/regional and is reserved only for prostate cancers by SEER. This combined code for stage is used for this study and has been recoded as a binary dichotomized variable. In reviewing the variable stage of Table 20, it is evident that a majority of men in both groups (96%) were diagnosed with localized/regional or early stage disease (χ^2 1796.6 df 4, $p < 0.0001$).

Also for the variable grade, 93.5% of the men of both races were a grade II defined as a Gleason score between 5-7 (χ^2 50, df 1, $p < 0.0001$). Further, the screening group is slightly more likely than the diagnostic group to receive a diagnosis of grade II (OR 1.25, 95%CI 1.17- 1.32).

When reviewing the categorical variable marital status for this elderly population, it is noted that for all marital categories, a greater proportion of men were in the dPSA group. The greatest variance is seen among men who were separated with 62% among the dPSA group and 38% among the sPSA group (χ^2 73, df 5, $p < 0.0001$). The second

greatest variance occurred among men in both the single/never married and divorced category (59% dPSA: 41% sPSA and 58% dPSA: 42% sPSA respectively). Interestingly, men who were married demonstrated the least amount of variance among groups. This same trend is seen throughout the literature where married men trended toward obtaining more screening PSA tests than men without a significant other.

Table 21 shows the distribution of socioeconomic variables by group including summary statistics and significance. Statistically significant differences exist within all categories. For example, the mean for men of the screening group was only slightly less than the mean of the diagnostic group for lower education whereas the mean for men attending higher education levels was greater for the sPSA group than the dPSA group. In addition, the median income for the screening group was just greater than the diagnostic group and statistically equivalent (see Table 21).

Overall, differences among group characteristics for the various treatments men received do not vary greatly. In fact, they coincide very well with Table 18 which shows treatments by race. For example, the majority of men in both groups shared the first three treatment choices of no radiation, radiation beam, or radioactive implants (sPSA 89% and dPSA 89.4%) with only a small portion choosing a combination of external beam plus a radioactive implant (7% for both groups; $\chi 2$ 287, df 9, $p < 0.0001$). Over 97% of screened men and 96% of non-screened men elected not to have any sequence of combined radiation beam with surgery as their treatment choice. Recall that the variable radiation and surgery were also dichotomized either as a “1” a man had some combined therapy or a “0” defined as a man chose not to have any combination of surgery and radiation.

Table 20. Socioeconomic Status by Group (Percent by zip code Census Tract 2000).

Group	sPSA						dPSA						Before p-score adjustment	
Percent by zip code (Census Tract 2000)	**N**	**N non missing**	**Mean**	**Std. Dev.**	**Min**	**Max**	**N**	**N non missing**	**Mean**	**Std. Dev.**	**Min**	**Max**	**N Total**	**Mean**
	32,210						**37,854**						**70,064**	**p-value**
														t-tests
Non High School Graduate		30,974	16	10	0	100		36,333	17	11	0	94		**<.0001**
High School only		30,974	26	10	0	80		36,333	27	10	0	80		**<.0001**
Some College Education		30,974	29	7	0	100		36,333	28	7	0	100		**<.0001**
College Education (4 years)		30,974	30	17	0	94		36,333	28	17	0	94		**<.0001**
Median Income		29,620	$38,396	$16,097	$7	$129,661		35,010	$37,101	$15,800	$7	$129,661		**<.0001**

When reviewing surgery as a treatment option, a high percentage of men who had surgery during one of the time periods prior to 1997 or after 1998 for the coded variables Site Specific Surgery (1983-1997) or Surgery of Primary Site (1998 +) and very small percentages for all surgery types combined. Therefore, the two variables were transformed and re-coded as binary as previously described. However, for purposes of detailing variance Table 22 shows where this variance occurred between groups. For example, men who chose radical prostatectomy with lymph node dissection (dPSA 6.2% and sPSA 2.8%) show an overall statistically significant difference between groups ($\chi^2$1493, df 17, $p < 0.0001$). Table 22 further describes variance in the choice of no cancer-directed surgery of which almost half of the men in the screening group and a third of the men in the diagnostic group chose (42% and 36%). A majority of men among both groups who elected to have surgery chose radical prostatectomy with overall significant differences in both groups (χ^2 286, df 16, $p < 0.0001$).

For hormone therapy, Table 22 shows a very high percentage of men from both groups electing not to receive hormones 6 months leading up to their first PSA test (99% and 94% respectively). However, this percentage drops significantly during the following 6 months afterwards where only 20% of the screening group and 65% of the diagnostic group do not take hormones. In addition, group differences exist in the distribution of men taking hormones during the same month as their PSA and being diagnosed (χ^2 491, df 1, $p < 0.0001$). Expectantly and perhaps due to symptoms, the percentage of men in the dPSA group receiving hormones during the 6 months following their initial PSA rose

Table 21. Study Group Characteristics by Treatment.

Group Characteristics by Treatment		Group	
		sPSA	dPSA
		n (%)	n (%)
Radiation	None	15,122 (47)	19,339 (51)
	Radiation Beam	8,685 (27)	10,096 (26.7)
	Radioactive implants	5,006 (15)	4,412 (11.7)
	Combination Radiation beam/implants	2,312 (7)	2,596 (7)
	Recommended, unknown if administered	342 (1)	440 (1.2)
	Unknown	339 (1)	508 (1.3)
Radiation sequence with surgery	No Radiation and/or cancer-directed surgery	31,438 (97.6)	36,491 (96.4)
	Radiation after surgery	683 (2)	1,229 (3.3)
Site Specific Surgery (1983-1997)	men part of next sequence SXPRIM1 (1998+)	28,439 (88.3)	29,539 (78)
	No surgical procedure	172 (0.53)	361 (1)
	Incisional, needle or aspiration biopsy of primary site	1,936 (6)	3,496 (9.2)
	Unknown	7 (0.02)	103 (0.30)
	TURP, Cryoprostatectomy w/o lymph node	328 (1)	1,143 (3)
	Radical Prostatectomy w/o lymph node	318 (1)	535 (1.4)
	Radical Prostatectomy with lymph node	906 (2.8)	2,346 (6.2)
Surgery of primary site (1998+)	men part of previous sequence SSSurg (1983-1997)	13,832 (43)	18,212 (48)
	No cancer-directed surgery	13,375 (41.5)	13,525 (35.7)
	TURP, NOS	140 (0.43)	187 (0.5)
	TURP, cancer incidental finding during surgery; benign	909 (2.8)	1,103 (2.9)
	TURP with cancer finding	307 (1)	460 (1.2)
	Cryoprostatectomy	100 (0.3)	124 (0.33)
Group Characteristics by Treatment		**Group**	
		sPSA n(%)	**dPSA n(%)**
Surgery of primary site (1998+) continued	Radical Prostatectomy	3,226 (10)	3,799 (10)
	Unknown	209 (0.65)	303 (0.8)
Hormone at time of diagnosis	No	31,755 (98.6)	35,566 (94)
	Yes	0 (0)	554 (1.5)
Hormone 1-6 months after diagnosis	No	6,487 (20)	24,596 (65)
	Yes	0 (0)	4,828 (13)

almost 9 times over those men receiving hormones during the same month as their PSA (13% vs. 1.5%). In addition, men in the screening group waited until taking hormones

until greater than 6 months after their PSA and diagnosis. Finally, group differences in the distribution of hormones from 1-6 months were significant ($\chi 2$ 1229, df 1, $p <$ 0.0001). Group and race summary statistics were examined for twelve previously defined comorbid conditions (Klabunde, Legler et al., 2007). The twelve comorbid conditions were assessed from hospital claims and physician claims beginning when a man became a Medicare enrollee and through a one year period until he turned 66 years old. All comorbid indices were summated according to the formula,

$$\Sigma^{12}_{i=1} = (X_1Y_1 + X_2Y_2 + X_3Y_3 \ldots + \ldots X_{12}Y_{12})$$

where X is the weighted coefficient and Y is the comorbid condition. The comorbid condition is defined as either being present (value 1) or not being present (value 0) (Klabunde, Legler et al., 2007). In looking at group comparison, note that statistical values were determined for the ratio of men among the dPSA group to men among the sPSA group (dPSA/sPSA). In other words, each odds ratio has been determined for the likelihood that men of the dPSA group would have the comorbid condition present. The same method is applied to race by comorbid condition where African American men are the numerated group. In all cases, odds ratios show that the dPSA group was more likely than the sPSA group to have any of the conditions. For example, when looking at whether a man had a previous heart attack (old myocardial infarct), men among the dPSA group were 1.4 times more likely than men of the sPSA group to report this condition (OR 1.41, 95%CI 1.25-1.59, $p < .0001$). With the exception of having a prior heart attack and rheumatologic processes, African American men within the dPSA group experienced the same trend (see Table 23). This may be explained by the fact that men who receive

results positive for cancer from a diagnostic PSA test could include greater proportions of unhealthier African Americans (have more comorbid conditions) and/or those who may not participate in regular annual health screening programs (Robbins et.al, 2000; Pinsky et.al, 2008).

Of particular interest, Table 23 shows that for the variables dementia and chronic renal failure, the dPSA group and African American men were nearly three times more likely to have the condition than their Caucasian counterparts. With the exception of rheumatologic processes, all comorbid conditions were statistically significant for the dPSA group before adjusting for propensity scores (p-score). As for race, all comorbid conditions except having had a recent heart attack, chronic obstructive pulmonary disease (COPD), and a rheumatologic disease were statistically significant for African Americans having the condition present.

Statistical Modeling

Logistic and Cox Regression: Before Propensity Analysis

Select outputs from the logistic regression model for the full population sample of 72,777 men before a propensity analysis was performed are shown below. Complete output tables for both the logistic and Cox regression models are found in Appendix A (see Appendix A). These two models are compared to logistic and conditional Cox regression models that do include a propensity analysis for evaluating the effects of using p-score adjustments. There were 32,210 screened men, 37,854 non-screened men, and 5,470 missing cases leaving a total of 67,307 men for this final analysis.

Table 22. Summary Statistics of Group and Race by Comorbid Condition.

	Group					Race				
	dPSA/sPSA					AA/Caucasian				
Comorbidity	**OR**	**95%CI**	**χ^2**	**df**	**p-value**	**OR**	**95%CI**	**χ^2**	**Df**	**p-value**
Previous Myocardial infarct	1.41	1.25-1.59	31.3	1	<.0001	0.666	0.53-0.842	11.7	1	0.001
Myocardial infarct	1.18	1.03-1.36	5.7	1	0.017	1.092	0.873-1.37	0.59	1	0.442
CHF	1.79	1.62-1.99	130	1	<.0001	1.75	1.53-1.99	69.4	1	<.0001
Peripheral Vascular Disease	1.33	1.19-1.48	26.9	1	<.0001	1.7	1.47-1.97	51	1	<.0001
Cerebrovascular Disease	1.33	1.23-1.45	49.7	1	<.0001	1.31	1.16-1.47	18.8	1	<.0001
COPD	1.32	1.25-1.39	94	1	<.0001	1.07	0.978-1.17	2.16	1	0.142
Dementia	2.78	1.85-4.19	26.2	1	<.0001	2.74	1.81-4.15	24.5	1	<.0001
Paralysis	1.97	1.4-2.75	16.2	1	<.0001	3.08	2.15-4.4	41.9	1	<.0001
Diabetes	1.18	1.11-1.25	32.3	1	<.0001	2.23	2.06-2.39	462	1	<.0001
Diabetes with Sequelae	1.22	1.075-1.38	9.54	1	0.002	2.45	2.1-2.86	136	1	<.0001
Chronic Renal Failure	2.65	2.13-3.28	83.8	1	<.0001	3.17	2.55-3.93	123	1	<.0001
Rheumatologic process	1.15	0.98-1.35	2.98	1	0.084	0.766	0.57-1.029	3.2	1	0.076

Table 24 shows the number of men that were included in the analysis and those that were not. The outcome variable for this model is mortality where a value of "1" is coded as dead and a value of "0" coded as alive with censoring applied at the study cut-off date of December 31, 2005 for all Cox modeling. Also, categorical variables were entered in all modeling with the first level being assigned as the reference indicator variable. For example, the categorical variable **race** is coded binary with Caucasian men assigned a value of "1" and African American men a value of "2" and with Caucasian being considered the first level and therefore entered as the reference variable. The overall model coefficients are shown to be significantly different at entry ($p<.0001$). Further, model summary coefficients do not explain much of the categorization (Cox & Snell R^2 3.7% and Nagelkerke R^2 13.3%). The classification table shows the model only correctly predicted 60 deaths and incorrectly predicted 15 (see Table 24).

Select outputs from the Cox regression model for the non-propensity analysis are provided later in this chapter. Of the total available 67,307 men, 64,695 were censored because they were still alive at the study cut-off date of December 31, 2005. The total number of deaths included 2,612 men with 5,470 cases removed. Also, overall model coefficients from Cox regression to be statistically significantly different for each of the entry steps ($p<.0001$) are provided. In addition, select outputs from both the logistic and Cox regression models for the sample population without use of a propensity analysis are illustrated later as well. The logistic regression model without p-score adjustment resulted in statistically significant differences for screening tests and being African American ($p = .001$, $p = .015$) with the non-screened men being 17% more likely to die than the

Table 23. Select Outputs from the Logistic Regression Model: Non-Propensity Analysis.

Case Processing Summary							
*unweighted cases				n	Percent		
selected cases		Included in Analyis		67,307	92.5		
		Missing Cases		5,470	7.5		
		Total		72,777	100		
Unselected cases				0	0		
Total				72,722	100		
a. if weight is in effect, see classification table for the total number of cases							
Omnibus Tests of Model Coefficients							
		Chi-square	Df	Sig.			
Step 1	Step	2551.208	37	0			
	Block	2551.208	37	0			
	Model	2551.208	37	0			
Model Summary							
Step	-2 Log likelihood			Cox & Snell R Square	Nagelkerke R Square		
1	19543.639[a]			0.037	0.133		
a. Estimation terminated at iteration number 7 because parameter estimates changed by less than .001.							
Classification Table[a]							
		Observed			Predicted		Percentage
					Mortality		Correct
					0	1	
Step 1		Mortality	0		64,680	15	100
			1		2,552	60	2.3
		Overall Percentage					96.2
a. The cut value is .500							

screened group (OR 0.853) and African American men were 19% more likely to die than Caucasian men (OR 1.194) (see Table 25 and Table 26). However the Cox regression model with no p-score adjustment reports no statistical differences in screening

Table 24. Select Outputs from the Cox Regression Model: Before Propensity Analysis.

Case Processing Summary									
		n	Percent						
	event[a]	2,612	3.6						
	censored	64,695	88.9						
	Total	67,307	92.5						
	cases with missing values	5,470	7.5						
	cases with negative time	0	0						
	cases censored before the earliest event in a stratum	0	0						
	Total	5,470	7.5						
Total		72,277	100						
a. Dependent Variable: survival time recode (total # of months)									
Omnibus Tests of Model coefficients[a]									
neg.2 Log Likelihood		overall (score)		change from previous step			change from previous block		
	chi^2	df	sig.	chi^2	df	sig.	chi^2	df	sig.
50706.85	1830.3	37	0	1387	37	0	1387	37	0
a. beginning blok number 1> method = enter									

Table 25. Select Outputs from Logistic and Cox Regression Models: Before Propensity Analysis.

Regression Outputs for Screening and African American Men: Before Propensity Analysis						
	B	**S.E.**	**Wald**	**df**	**Sig.**	**Exp (B)**
Logistic Model						
Being screened	-.159	.048	10.929	1	.001	.853
Being African American	.177	.073	5.869	1	.015	1.194
Cox Regression Model						
Being Screened	-.053	.047	1.289	1	.256	.948
Being African American	.134	.070	3.650	1	.056	1.144

and slightly trends toward a greater mortality rate when being African American (p = .256 and p = .056 respectively).

The Propensity Analysis

The first step in performing a propensity analysis involved running a multivariate logistic regression model using the treatment or intervention, a screening PSA test in this case, as the dependent variable against all relevant covariate independent variables and comorbid conditions to calculate individual p-scores for all subjects. Recall that the p-score simulates randomization by adjusting for observed selection bias through matching (Rosenbaum & Rubin, 1983; Rubin 2002; D'Agostino, 1998). The results of this model are saved as a new data set and used as an input file during the matching phase described below.

Once the propensity scores were calculated one-to-one matched pairs were created from men in the screened group (sPSA = 1, "yes') to men from the non-screened group (sPSA = 0, "no"). A matching macro designed to perform propensity score matching using SPSS syntax was applied for this step. Original basic core elements of the program were created by Raynald Levesque (http://pages.infinit.net/rlevesqu/). Levesque's program was adapted for use with propensity matching by John Painter (www.unc.edu/~painter). Using the macro requires input from researchers, namely input of the new data file created in the first step of the propensity analysis described above where the estimated p-scores were already computed. The matching macro uses a similar technique known as Mahalanobis metric matching where matches are created within a defined propensity score caliper width of 0.2 standard deviations on the estimated p-score

of the treatment case (Rubin, 2002). This technique has been referred to as a greedy procedure because once a match is found and a pair created, that pair is removed from future match considerations. It has been reported that greedy matching algorithms have shortcomings of their own, in that studies with greater numbers of cases than controls both of which having high p-scores may result in high numbers of poor matches (Luo, Gardiner, & Bradley, 2009).

The current study was not subject to these pitfalls as the beginning total sample population was sufficiently large enough to trim all poorly matched pairs leaving only resultant one-to-one pairs of equal numbers and nearly perfectly matched in p-scores. Further, an additional self-imposed study threshold tolerance of ±5 percent difference in propensity scores was set with pairs falling outside the criterion being trimmed from the sample. Therefore, by applying an accepted published restricted caliper of estimated p-scores being within ±0.2 standard deviations among pairs along with a self-imposed maximum difference in estimated p-scores of ±5 percent, it is believed that the resultant matched pairs were adequate for this study.

After matching is completed, the macro sorts the total sample population by all available treatment cases (sPSA) and starting with the first case, searches from the pool of all possible non-treatment cases (dPSA) for either an exact propensity score match or a match having the closest p-score. Once a match is found, the pair is removed from further searches to prevent possible repeat matches. This process continues until each treatment case has been assigned a match with a non-treatment case.

Finally, a new dataset of matched cases to non-cases is created and stored as a separate file. The matched pairs created from the macro are shown with the black line representing the sPSA group and the white line the dPSA group in Figure 6. Propensity scores are plotted on the y-axis in ascending order beginning with zero and finishing at a value close to one. Imbalance in covariate distributions appears as divergence in the two lines indicating a poor match. The number of matched pairs is shown across the x-axis. From the beginning pool of 72,777 men, the matching macro found 61,948 matches thus creating 30,974 pairs (see Figure 6). The next step was to observe the quality of the matching for noting incomplete or inexact matching. Incomplete matching occurs if not all case subjects were matched and inexact matching occurs when if a match is formed by two dissimilar subjects (Rubin, 2002). It is observed in Figure 6 that the two curves begin separating near 25,000 after which they tend towards an inverse relationship possibly indicating incomplete or inexact matching and/or presence of additional unknown biases caused from unobserved covariates, in both cases obviously poor matches. These poorly matched pairs caused by either incomplete or inexact matching and the possible presence of unknown covariates could lead to problematic inferences and therefore decisions must be cautiously made for removing them from the study population (Rubin, 2002) (see Figure 6). For these reasons and because the numbers of matched pairs remains large, it was decided to trim an additional 5,974 pairs as they exhibit poor matching and their p-scores fell outside study criteria of ± 5 percent difference and outside the predefined caliper width of ±0.2 standard deviations. Therefore, the final trimmed matched sample of 25,000 pairs chosen for the remaining statistical testing and comparisons of this study.

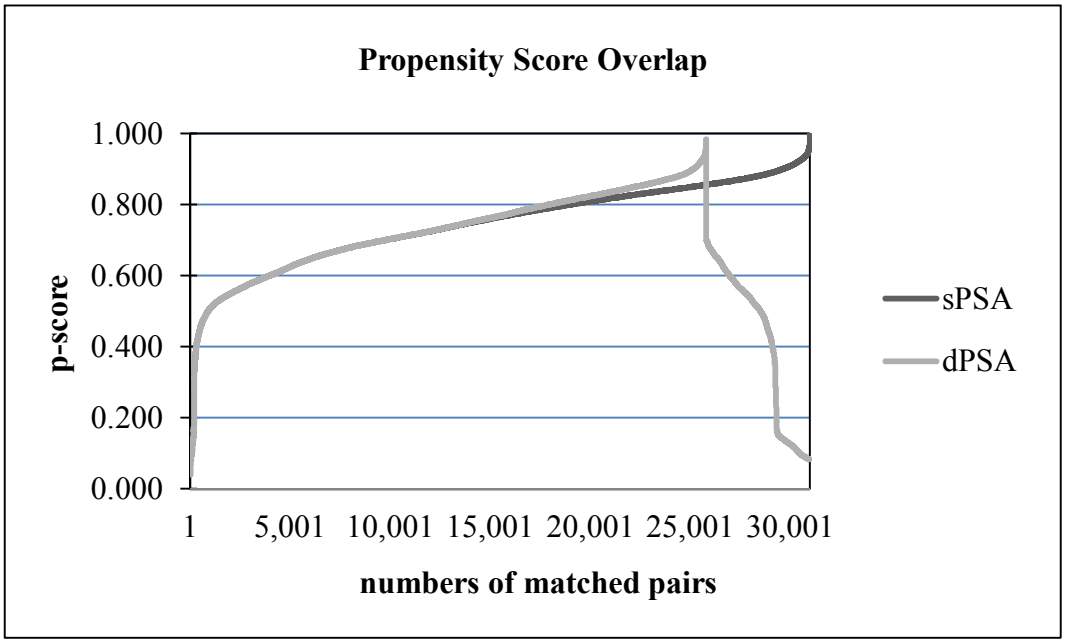

Figure 6. Illustration of Propensity Score Match and Overlap.

A final step in using a propensity analysis is to consider stratification of the sample into quintiles, especially in studies where matched pairs may be incomplete or inexact or there are multiple controls matched to a single case. Forming quintiles based on the closeness of propensity score allows a ranking of the pairs by setting boundaries that could provide additional detailed information and thus possible improvements in balancing covariate distribution and end-point outcomes. Additional improvements may be observed because now pairs within each quintile are compared against each other across a smaller sample size where the p-scores are closer in value than those observed over the full sample (Rubin, 2002). Although the current study retained a sufficiently large number of nearly equally matched pairs (25,000 pairs) and arguably, forming quintiles may not be necessary, however, benefits of creating quintiles are the ability to

compare results from within each and compare to overall model results. A potential drawback is that as the sample data are divided into quintiles, the count per race may be reduced, especially for under-represented minority groups. As expected, the numbers of African American men of this study did decline within each quintile 1 through 5. For example quintile 1 contains 8,960:2,558 Caucasians to African Americans and for quintiles 2 through 5 the ratios are 6,992:1,092, 10,780:716, 7,810:90, and 10,992:10, respectively.

Creating the quintiles was done arbitrarily with care taken when examining the data in Figure 6 above. Points of inflection in the graph were chosen as boundaries for each quintile and can be seen in Figure 7. The vertical parallel lines in Figure 7 illustrate where these break points occurred and serve to define quintile samples. For example, the first quintile was chosen at a point occurring just after the first shoulder as the two curves begin to rise and then flatten out again. In particular, quintile 1 contains 5,759 matched pairs. The remaining 4 quintiles were defined the same way with quintiles 2 through 5 containing 4,042 pairs, 5,748 pairs, 3,950 pairs, and 5,501 pairs respectively. The first quintile is composed of the lowest p-scores and represents men least likely to be screened, whereas the fifth quintile is composed of the highest p-score representing men most likely to be screened.

After completing the propensity analysis, further examination of whether or not p-score adjustments are helpful can be evaluated by comparing the absolute standardized differences in before and after p-score adjustment. Comparing before and after estimated probabilities and calculating absolute standardized differences are proven methods for

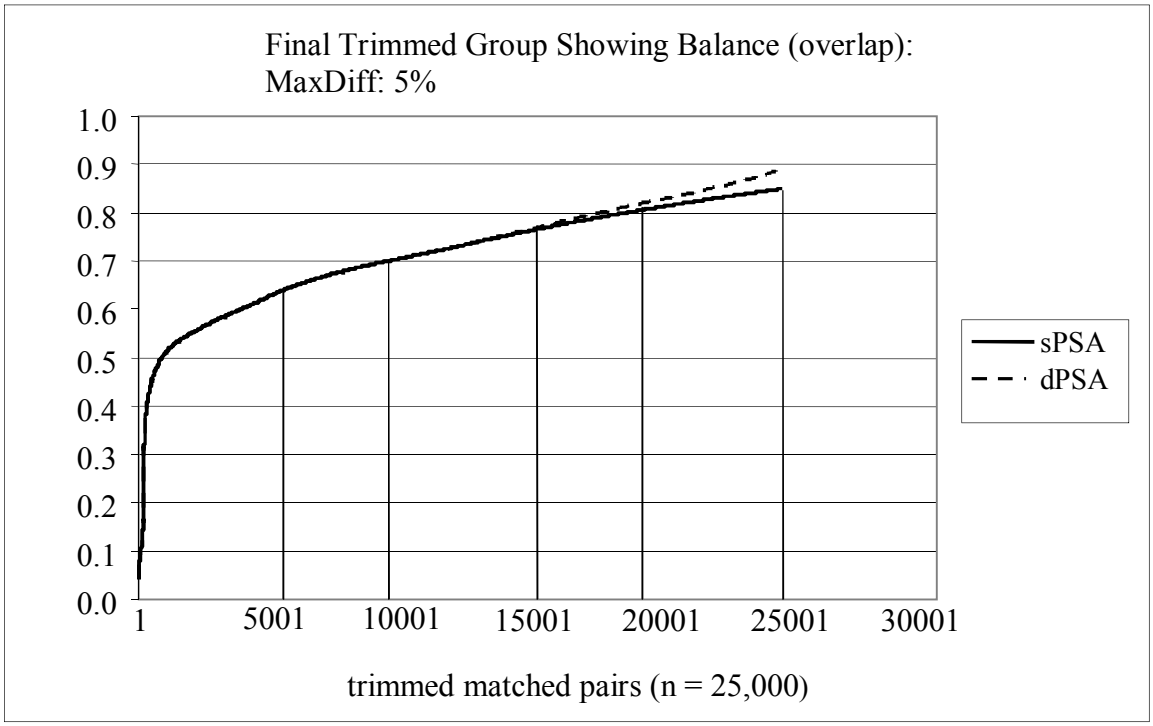

Figure 7. Final Trimmed Matched Pairs.

demonstrating balance of groups and overlap of covariates.

Comparing standardized differences may be an improved method for assessing bias among individual covariates across groups rather than individual tests of significance that only compare the means of those covariates (Rubin, 2002; Love, 2001). For example, results from the multivariate logistic regression model without p-scores are compared with results from the logistic model with p-scores for the 25,000 matched pairings. A compilation showing **before** and **after** estimated probabilities for having a screening PSA test versus not having a screening PSA test and **before** and **after** calculations of the absolute standardized differences is listed below. Calculating the absolute standardized differences for continuous covariates is simply the difference in means in the two groups

divided by the standard deviation of the groups. And for the categorical variables, the absolute standardized difference is the difference in proportions of the two groups divided by the standard deviation of two proportions (Rubin, 2002). Further, it is common to express standardized differences in percentages with values within ±10% being the normally accepted threshold limit (Rubin, 2002; Love, 2001).

Of the 39 predictor variables 36 were significantly different ($p < 0.05$) before matching which implies for those observed characteristics men were dissimilar resulting in unexplainable variance because of the presence of unknown biases (see Table 27). After matching, only 10 predictor variables remained significantly different and of those 10 remaining different, three were from the categorical variable age (men 66-69 years, 80-84 years, and 85 or older), one from the variable **grade**, two from the categorical variable **marital status** (single/never married and married), and three from the variable **treatment** (no radiation, radioactive implants, and surgery). The 10^{th} variable remaining statistically different after p-score adjustment was **median income** from the socioeconomic variables.

The variable **hormone** was statistically different before matching whereas afterwards, its resultant value was a constant as no men from the final matched data set had taken hormones (value = 0, "no"). In addition, the distributions for all the comorbid conditions became balanced after matching (see Table 27). Overall, it appears that using propensity matching has removed much of the bias between screened and non-screened men and for race. However, it is noted that for the categorical variable **age**, some unknown biases may still remain for three of the five categorical levels. Knowing that

Table 26. Variable Characterization of Significance and Percent Absolute Standardized Differences for Before and After Matching.

Having a Screening PSA test	**Before Match**		**After Match**	
	p-value	**Abs. Std. Diff (%)**	**p-value**	**Abs. Std. Diff (%)**
Race	<.0001	46.3	0.385	0.90
Age				
66-69 yrs.	<.0001	23.5	<.0001	0.22
70-74 yrs.	<.0001	10.5	0.770	0.84
75-79 yrs.	<.0001	11.4	0.174	2.2
80-84 yrs.	<.0001	3.5	0.001	3.3
85+ yrs.	<.0001	1.3	0.023	0.0
Disease Extent				
Grade	<.0001	22.6	0.044	7.5
Stage	<.0001	129.3	1.000	0.0
Marital status				
Single/never married	<.0001	18.74	0.002	5.5
Married	<.0001	5.63	0.038	4.42
Separated	0.301	31.4	0.796	7.0
Divorced	0.833	17.5	0.698	3.2
Widowed	<.0001	2.87	0.968	3.0
Unknown	<.0001	0.42	0.544	0.2
Treatment Options				
None	<.0001	8.4	<.0001	3.8
Radiation beam	<.0001	11.1	0.353	6.1
Radioactive implant	<.0001	0.7	<.0001	0.89
Radiation/implant combination	<.0001	1.2	0.297	0
Radiation recom. unknown if taken	0.023	1.84	0.903	0.90
Radiation/surgery combined	<.0001	7.4	0.118	1.5
Having any surgery	<.0001	46.7	0.006	5.1
Hormones	<.0001	61.2	Constant	0

Table 27: continued.

Having a Screening PSA test	Before Match		After Match	
Social Economic Variables				
Non-high school graduate	<.0001	9.5	0.876	6.0
High school graduate	<.0001	10.0	0.923	6.0
Some college	<.0001	14.3	0.518	0.0
4 yrs. College	<.0001	11.76	0.568	5.8
Median income	<.0001	12.51	0.022	4.9
Comorbid Conditions				
Previous myocardial infarct	<.0001	4.38	0.253	1.0
Myocardial infarct	0.017	1.85	0.934	0.08
CHF	<.0001	9.1	0.434	0.7
Peripheral vascular disease	<.0001	4.1	0.210	1.2
Cerebrovascular disease	<.0001	5.7	0.114	1.5
COPD	<.0001	8.4	0.063	1.1
Dementia	<.0001	4.0	0.378	0.80
Paralysis	<.0001	3.1	0.753	0.28
Diabetes	<.0001	4.9	0.149	1.5
Diabetes with sequelae	0.002	2.4	0.939	0.07
Chronic renal failure	<.0001	7.13	0.893	0.12
Rheumatologic process	0.084	1.33	0.243	1.1

age is a predictor of mortality in and of itself, it was warranted to examine the variable separately for evaluating its effects on mortality among race and prostate cancer. Therefore, a comparison evaluation was performed by creating an age matched - propensity matched analysis and is detailed later.

Figure 8 is a plot of the standardized differences presented in Table 27 where it is noted that 16 of the 39 covariates resulted in differences greater than ±10 percent before the propensity analysis while all 39 met threshold limits after the propensity analysis was applied (see Figure 8). The white dots form a line showing covariate imbalance before p-

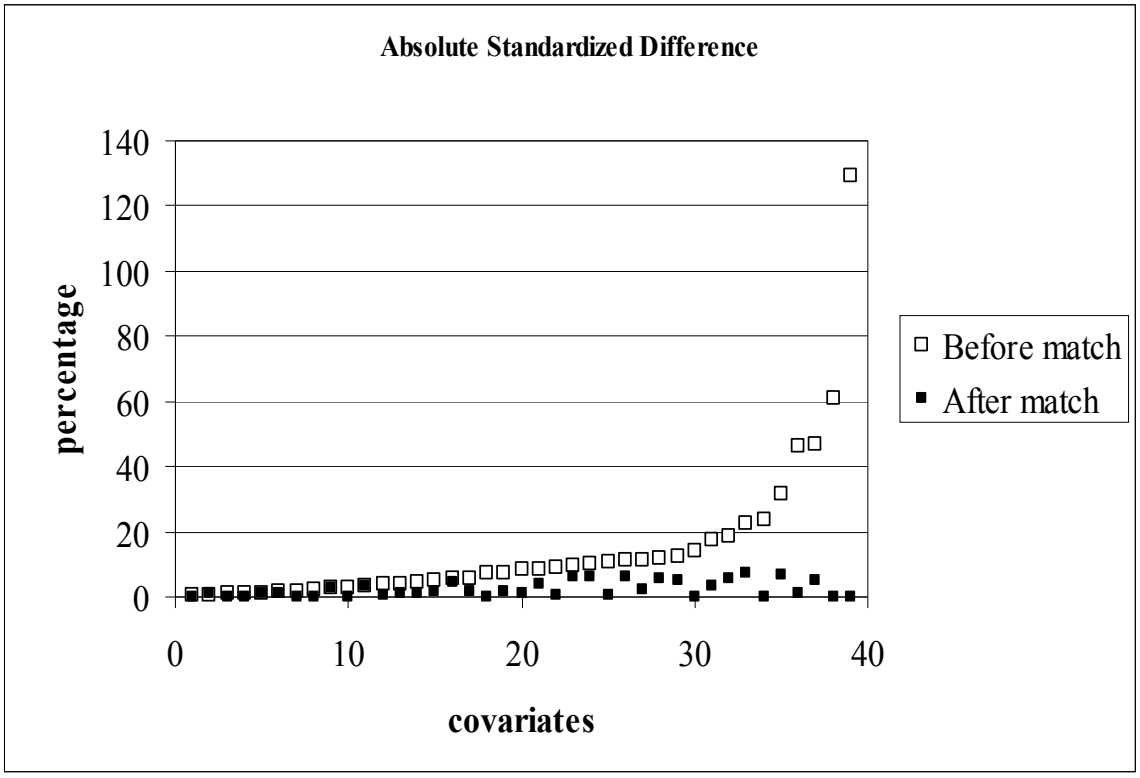

Figure 6. Absolute Standardized Differences before and after Propensity Matching.

score adjustment as noted in the amount of deviation away from the zero line, whereas the black dots form a line showing improved balance after adjusting with p-scores as they collectively align closer to the zero marker suggesting that most selection bias has been removed. Obviously standardized differences of zero reflect perfect balance in groups and overlap in covariate distribution.

Logistic and Cox Regression: After Propensity Analysis

At this point, the propensity analysis is complete and more traditional statistical methods may be applied and assessed. For example, logistic regression and conditional Cox regression models using propensity score adjustments were generated for the full

data set of 25,000 matched pairs (labeled FM) as well as for each quintile. Results from the full data set model (FM) along with results from the models for each quintile were compared to the full models developed without a propensity analysis applied.

Conditional Cox regression models allow censoring for time to event to occur and can account for dependency of matched pairs by using a dummy variable created for each pair. For example, a dummy variable called "pairs" was created where each pair was numbered in sequence and ordered according to the numbering. Pairing variables were created for the full sample data set (FM) and for each of the quintile data sets.

Selected summary statistics for the logistic regression and conditional Cox regression models are shown for the FM data and for all quintiles (Q1-Q5) respectively. Complete output results from each model appear in Appendices B through G. Panel A contains model summary statistics of the Cox & Snell R^2 and Omnibus Model Coefficients from the logistic regression model. The square of the correlation coefficient, R, is used in linear regression as a tool to describe the amount of variance accounted for by the model. The Cox & Snell R^2 are similar to the correlation coefficient of linear regression models except that because the results are binary in logistic regression models, these coefficients may be viewed, cautiously, as being related to a proportion of how well the model categorized or classified mortality. The overall model fit for each quintile also shows significant differences as may be expected in models containing a majority of predictor variables contributing little or no significance to the overall model (see Table 28). Panel B of Table 28 shows model coefficients from the conditional Cox regression model. In particular, the FM model and all five quintiles remained statistically different

Table 27. Model Summary and Omnibus Coefficients: A - Multivariate Logistic Regression, B - Conditional Cox Regression Models for Quintile.

A: Logistic Regression Model Summary										
Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square							
FM	13312.94a	0.014	0.058							
Q1	3001.252a	0.034	0.133							
Q2	2138.297a	0.019	0.076							
Q3	3366.457a	0.015	0.058							
Q4	2035.308a	0.009	0.039							
Q5	2586.141a	0.007	0.031							
A: Logistic Regression Omnibus Tests of Model Coefficients										
		Chi-square	df	Sig.						
FM	Step, Block, Model	713.126	33	0						
Q1	Step, Block, Model	399.392	36	0						
Q2	Step, Block, Model	153.657	35	0						
Q3	Step, Block, Model	178.886	34	0						
Q4	Step, Block, Model	72.722	33	0						
Q5	Step, Block, Model	73.311	32	0						
B: Conditional Cox Regression Omnibus Tests of Model Coefficients[a]										
-2 Log Likeli	Overall (score)				Change From Previous Step			Change From Previous Block		
	Chi-square	df	Sig.		Chi-square	df	Sig.	Chi-square	Df	Sig.
FM 1006.15	159.52	31	0		180.21	31	0	180.214	31	0
Q1 205.389	73.46	34	0		95.437	34	0	95.437	34	0
Q2 87.83	62.43	31	0.001		88.229	31	0	88.229	31	0
Q3 229.242	56.66	31	0.003		66.038	31	0	66.038	31	0
Q4 118.969	52.081	32	0.014		66.795	32	0	66.795	32	0
Q5 153.410	60.061	26	0		75.328	26	0	75.328	26	0
a. Beginning Block Number 1. Method = Enter										

from the overall step through each change in entry. Summary results from the logistic regression model for the FM data set and for each quintile show that 50,000 men had no missing data and 1,577 men were observed as dying with the model predicting only 4 deaths, 3 of which were correctly predicted as being dead. In looking at quintile 1, there were 11,518 men (5,759 pairs) and zero missing cases among which 382 men were

observed as having died with the model's predicted comparison of nine deaths. Of these nine, the model correctly predicted seven and incorrectly listed two men as dead with the remaining 380 men going undetected. The model's overall percentage of correct mortality prediction was 96.7 percent. This is most likely a ceiling effect in that it may be the same result laymen would predict merely by stating that every man would live. Ceiling effects are sometimes difficult to improve upon in future modeling. The remaining quintiles show similar results (see Table 29).

Additional summary statistics from the logistic regression and conditional Cox regression models for the FM and each quintile show no significant differences in race and mortality; however, regarding being screened, slight statistically significant differences were noted among screening distributions and mortality; with non-screened men ($\beta = -0.140$) being approximately 0.87 times as likely to die (OR=0.87, p=.007). Results for the quintile data resulted in no statistically significant differences in mortality between screened and non-screened (sPSA vs. dPSA) men for all quintiles with the exception of number three which resulted in statistically significant differences at p=.004. It is noted that within quintile 3, screened men were almost 0.26 times as likely to die (OR 0.743) or similarly, non-screened men were almost 1.35 times more likely to die than screened men (OR 1/0.743) as indicated by a negative unstandardized beta coefficient (β) of -0.297. The beta coefficient represents the slope of a line showing direction of predictor distribution for significance with the odds ratio Exp (β) showing the impact of those differences. For example, a positive slope would have an odds ratio greater than one and a negative slope would have an odds ratio of less than one.

Table 28. Summary Classification for FM and Quintiles.

Logistic Regression

FM

Case Processing Summary		
Included in analysis	50,000	100
Missing Cases	0	0
Total	50,000	100

Classification Table

Block 1 : Method = ENTER

		Predicted		
		Mortality		
Observed		0	1	Percentage Correct
Mortality	0	48,419	1	100.0
	1	1,577	3	.2
Overall Percentage				96.8

Quintile 1

Case Processing Summary		
Included in analysis	11,518	100
Missing Cases	0	0
Total	11,518	100

Classification Table

Block 1 : Method = ENTER

		Predicted		
		Mortality		
Observed		0	1	Percentage Correct
Mortality	0	11,127	2	100
	1	382	7	1.8
Overall Percentage				96.7

Table 29: continued.

Quintile 2							
Case Processing Summary			**Classification Table**				
			Block 1 : Method = ENTER				
Included in analysis	8,084	100			Predicted		
Missing Cases	0	0			Mortality		
Total	8,084	100	Observed		0	1	Percentage Correct
			Mortality	0	7,825	0	100
				1	259	0	0
			Overall Percentage				96.8
Quintile 3							
Case Processing Summary			**Classification Table**				
			Block 1 : Method = ENTER				
Included in analysis	11,496	100			Predicted		
Missing Cases	0	0			Mortality		
Total	11,496	100	Observed		0	1	Percentage Correct
			Mortality	0	11,085	0	100
				1	411	0	0
			Overall Percentage				96.4

Table 29: continued.

Quintile 4							
Case Processing Summary			**Classification Table**				
			Block 1 : Method = ENTER				
Included in analysis	7,900	100			Predicted		
Missing Cases	0	0			Mortality		
Total	7,900	100	Observed		0	1	Percentage Correct
			Mortality	0	7,666	0	100
				1	234	0	0
			Overall Percentage				97
Quintile 5							
Case Processing Summary			**Classification Table**				
			Block 1 : Method = ENTER				
Included in analysis	11,002	100			Predicted		
Missing Cases	0	0			Mortality		
Total	11,002	100	Observed		0	1	Percentage Correct
			Mortality	0	10,715	0	100
				1	287	0	0
			Overall Percentage				97.4

The remaining quintiles of 2, 4, and 5 show similar results with no statistically significant differences in screened versus non-screened men and mortality. Regarding race and the logistic regression model, there were no statistically significant differences among race and mortality for the FM and all quintiles when using p-score adjustment (see Table 30). Of particular interest, the fifth quintile resulted in a large regression coefficient (slope β), a large standard error for the coefficient (S.E.), and a large p-value that may be attributed to the vast difference in the proportion of Caucasian men to African American men in the sample (10,992:10, Caucasian men: African American men, respectively).

Table 30 also shows similar results for the conditional Cox regression model with no statistically significant differences for the FM model and any of the five quintiles regarding men being screened and among race. However, quintile 5 resulted in a constant value for race and mortality with no other data reported, where again, it is believed that these extreme values and constancy for race of quintile five may be due to the low proportion of African American men in this sample (10,992:10).

AGE Matched Models: After Propensity Analysis

Because age is a known predictor of mortality and because initial model results within the sample population of this study may have retained unknown biases after the propensity analysis was applied, it was decided to examine age in a separate analysis using **age matched** and **propensity matched** pairings within quartiles. The fourth and fifth age category were combined because of too few men in the age group of over 85 years in an attempt to keep the number of men per number of predictor variables sufficient enough to reduce the chances of introducing new unknown biases from an

Table 29. Summary Statistics for Logistic and Conditional Cox Regression on FM and Quintiles on PSA Screening and African American Men: After Propensity Analysis.

Logistic Regression Output for Screening and African American Men						
	B	**S.E.**	**Wald**	**df**	**Sig.**	**Exp(β)**
FM						
being screened	-.140	.052	7.282	1	.007	.870
being African American	.058	.099	.342	1	.559	1.060
Quintile 1						
being screened	-.196	.108	3.321	1	.068	.822
being African American	.148	.159	.861	1	.353	1.159
Quintile 2						
being screened	-.101	.128	.618	1	.432	.904
Being African American	.339	.520	.424	1	.515	1.403
Quintile 3						
being screened	-.297	.102	8.407	1	.004	.743
being African American	.551	.375	2.155	1	.142	1.735
Quintile 4						
being screened	.075	.142	.277	1	.599	1.077
being African American	-.608	1.194	.259	1	.611	.545
Quintile 5						
being screened	-.086	.143	.358	1	.549	.918
Being African American	-16.443	14180	.000	1	.999	.000

Table 30: continued.

Conditional Cox Regression Adjusted for Matched Pairs on Screening and African American Men						
	B	**S.E.**	**Wald**	**df**	**Sig.**	**Exp(β)**
FM						
Being screened	-.001	.078	.000	1	.993	.999
Being African American	-.644	.369	3.040	1	.081	.525
Quintile 1						
Being screened	.019	.185	.010	1	.919	1.019
Being African American	2.918	4.258	.470	1	.493	18.506
Quintile 2						
Being screened	-.292	.316	.856	1	.355	.747
Being African American	-1.215	39.584	.001	1	.976	.297
Quintile 3						
Being screened	-.182	.251	.523	1	.469	.834
Being African American	-.981	21.664	.002	1	.964	.375
Quintile 4						
Being screened	.646	.891	.526	1	.468	1.909
Being African American	-9.760	71.167	.019	1	.891	.000
Quintile 5						
Being screened	.508	.660	.593	1	.441	1.663
Being African American				0[a]		

under-represented sample size. All matched pairings created previously from predetermined p-scores were maintained with subsequent formation of quartiles for age created by using the categorical levels of age. For example, men previously matched by p-score were kept for the age analysis if they were also of the same age category. If a pair was matched by p-score but not of the same age category, they were trimmed from the sample leaving only p-score and age matched pairings. Therefore, matched pairs were formed where men aged 66-69 years formed the first age quartile (AQ1), men aged 70-74 years formed AQ2, men aged 75-79 years formed AQ3, and all men over 80 years formed AQ4. In addition, men who were not paired by age in the first matched pairings were trimmed from the age quintiles. The resultant sample of age matched and propensity matched pairings for age categories contained 20,232 men (10,116 pairs). Table 31 is an output of frequency and percentages showing the results of the age quartiles.

Table 31. Frequency Count for Age Matched Quartiles.

Age Quartiles	Frequency	Percent	Valid Percent	Cumulative Percent
AQ1(66-69)	9,392	46.4	46.4	46.4
AQ2 (70-74)	7,058	34.9	34.9	81.3
AQ3 (75-79)	3,118	15.4	15.4	96.7
AQ4 (>80)	664	3.3	3.3	10
Total	20,232	100	100	100

The final trimmed and combined age quartiles were thus created as AQ1-AQ4 for men age 66-69 years, 70-74 years, 75-79 years, and over 80 years as shown in Figure 9. The figure illustrates the numbers of men within each age category decreasing for each age group with the majority being within the first and second age groups of 66-69 years

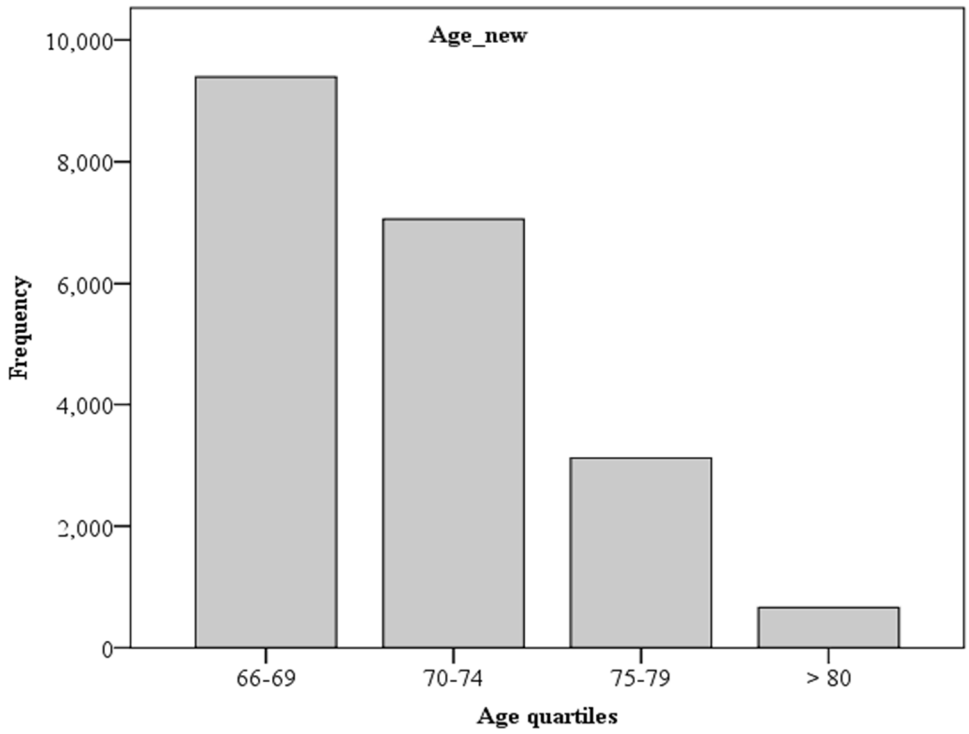

Figure 9. Final Bar Plot of Frequency Count for Age Matched Quartiles.

and 70-74 years. The last two age categories contained fewer men but remained a large enough sample to maintain statistical modeling providing sufficient results. Model summary and omnibus model coefficients from both the logistic and conditional Cox regression models appear in panel A and panel B below for each age quartile. Selected summary statistics from the logistic and conditional Cox regression model for the screened and non-screened group on mortality as well as for race on mortality for each **age** quartile are provided below with complete output tables presented in Appendices H through K.

In particular, Table 32 panel A shows that overall model coefficients from the logistic regression model were statistically significantly different for all quartiles with the

Table 30. Model Summary and Omnibus Coefficients for Age Quartiles: A: Logistic Regression and B: Conditional Cox Regression.

A: Model Summary from Logistic Regression												
Step	-2 Log likelihood		Cox & Snell R^2		Nagelkerke R^2							
AQ1	1698.70		0.007		0.041							
AQ2	1601.98		0.007		0.035							
AQ3	960.51		0.026		0.092							
AQ4	274.24		0.033		0.093							
A: Logistic Regression Omnibus Tests of Model Coefficients												
			Chi^2		df		Sig.					
AQ1	Step, Block, Model		65.739		29		0.00					
AQ2	Step, Block, Model		52.299		28		0.004					
AQ3	Step, Block, Model		82.214		28		0.00					
AQ4	Step, Block, Model		22.529		26		0.659					
B: Cox Regression Omnibus Tests of Model Coefficients[a]												
Likelihood	Overall (score)			Change from Prev. Step			Change from Prev. Block					
	Chi^2	df	Sig.	Chi^2	df	Sig.	Chi^2	df	Sig.			
AQ1 140.02	28.471	28	0.440	0	28	0.10	0	28	0.10			
AQ2 103.04	26.109	26	0.457	34.203	26	0.13	34.203	26	0.13			
AQ3 54.384	29.175	27	0.352	39.884	27	0.053	39.884	27	0.053			
AQ4 33.271	19.424	21	0.558	0	21	1.00	0	21	1.00			
a. Beginning Block Number 1 Model = Enter												

exception of the fourth for men over 80 years (p = .659) while Panel B of Table 32 shows no significant differences in coefficients for all age quartiles from the conditional Cox regression model.

Additional summary statistics for the classification outputs from the logistic regression model are shown in Table 33 for each age quartile on mortality. The table shows a ceiling effect for each quartile's correctly predicted overall mortality percentage of no less than 94.1% (AQ4). Summary statistics from both the logistic and conditional Cox regression model for each age quartile are presented later in the chapter. Results from the logistic regression model show no statistically significant differences in

Table 31. Logistic Regression Summary Classification for Age Quartiles.

Logistic Regression							
AGE Quartile 1							
Case Processing Summary			**Classification Table**				
			Block 1 : Method = ENTER				
Included in	9,392	100			Predicted		
Missing Cases	0	0			Mortality		
Total	9,392	100	Observed		0	1	Percentage Correct
			Mortality	0	9,214	0	100
				1	178	0	0
			Overall Percentage				98.1
AGE Quartile 2							
Case Processing Summary			**Classification Table**				
			Block 1 : Method = ENTER				
Included in	7,058	100			Predicted		
Missing Cases	0	0			Mortality		
Total	7,058	100	Observed		0	1	Percentage Correct
			Mortality	0	6,88	0	100
				1	176	1	.6
			Overall Percentage				97.5
AGE Quartile 3							
Case Processing	**Classification Table**						
			Block 1 : Method = ENTER				
Included in analysis	3,11	100		Predicted			
Missing Cases	0	0		Mortality			
Total	3,11	100	Observed	0		1	Percentage Correct
			Mortality	0	2,994	0	100
				1	123	1	.8
			Overall Percentage				96.1
AGE Quartile 4							
Case Processing Summary			**Classification Table**				
			Block 1 : Method = ENTER				
Included in analysis	664	100			Predicted		
Missing Cases	0	0			Mortality		Percentage
Total	664	100	Observed		0	1	
			Mortality	0	625	0	100
				1	39	0	0
			Overall Percentage				94.1

mortality among screened and non-screened men and among race and mortality for any of the four age quartiles. Regarding the conditional Cox regression model, Table 34 shows no significant differences in mortality for screening and race in all four age quartiles.

Table 32. Summary Statistics from Logistic and conditional Cox Regression for Age Quartiles on PSA Screening and African American Men: After Propensity Analysis.

Logistic Regression Output for Screening and African American Men						
	B	**S.E.**	**Wald**	**Df**	**Sig.**	**Exp (B)**
Age Quartile 1						
Being screened	-.088	.153	.332	1	.565	.916
Being African American	.165	.249	.438	1	.508	1.179
Age Quartile 2						
Being screened	-.122	.155	.617	1	.432	.885
Being African American	.546	.285	3.673	1	.055	1.726
Age Quartile 3						
Being screened	-.231	.191	1.471	1	.225	.794
Being African American	-.361	.610	.351	1	.554	.697
Age Quartile 4						
Being screened	-.115	.350	.109	1	.741	.891
Being African American	-.138	1.077	.016	1	.898	.871
Cox Regression Adjusted for Matched Pairs on Screening and African American Men						
	B	**S.E.**	**Wald**	**Df**	**Sig.**	**Exp (B)**
Age Quartile 1						
Being screened	.000	.243	.000	1	1.000	1.000
Being African American	.000	54.375	.000	1	1.000	1.000
Age Quartile 2	**B**	**S.E.**	**Wald**	**Df**	**Sig.**	**Exp (B)**
Being screened	-.076	.350	.047	1	.829	
Being African American	4.731	3.763	1.581	1	.209	113.39
Age Quartile 3						
Being screened	-.719	.622	1.338	1	.247	.487
Being African American	-5.51	5.535	.991	1	.320	.004
Age Quartile 4						
Being screened	.000	1.200	.000	1	1.000	1.000
Being African American	.000	12.920	.000	1	1.000	1.000

The Non-Cancer Group Analysis

The second part of this study included examining the same effects of screening PSA tests on men without prostate cancer. These men were pooled from the SUMDENOM files provided by the SEER-Medicare data linkage project. The NCI created this file from demographic and entitlement information for Medicare beneficiaries who do not have cancer. The file is created from a random 5 percent sample of Medicare beneficiaries residing in the same SEER areas and include years of eligibility, unique health insurance claim numbers (HIC), dates of birth, dates of death, sex, race, states of residency, enrollment in part A and/or Part B, and enrollment in HMOs.

The file contained 263,548 patient records among which 163,501 were immediately excluded because of not being either Caucasian or African American. Another 9,032 men were excluded for other various reasons that included either not being in both Part A and Part B of Medicare, being in an HMO, or having been treated for prostate cancer. Unfortunately, it is common for some men to either be clinically misdiagnosed from false positive screening tests that result in treatment or to start treatment without first having the cancer pathologically confirmed both of which may be a leading cause of over utilization of treatment. Final exclusions were men who had other malignancies diagnosed, men with incomplete or insufficient diagnoses, and men who had no validated date of death recorded leaving a sample population of 91,015 men. Further analysis of the sample population determined numerous cases with missing values. In particular, men with missing values in all variables were trimmed reducing the

sample population to 15,557 men. From this sample, there were a few men with missing values from the socioeconomic variables so it was decided to impute these missing values. Therefore, the final trimmed data set with imputed missing values resulted in a sample population size of 15,557 men.

The process for evaluating prostate screening effects for the non-cancer cases was the same as previously noted for the cancer cases in that, after sample selection, men were grouped according to the algorithm in Figure 4 above either as being screened (sPSA) or not screened (dPSA). After groups were formed, a traditional logistic regression with no propensity adjustment was performed as a base model in which to compare other models that did include a propensity analysis. The next step was to perform the propensity analysis on the final selected sample population of 15,557 men in the same manner as for the cancer cases namely, to calculate estimated p-scores, perform a match for creating pairs, and run both logistic and conditional Cox regression models for all subsequent model comparisons.

Demographics and Summary Statistics

Table 35 shows frequency statistics for group and race. Out of the total 15,557 men, there were 11,341 (72.9%) men from both races who elected to be screened regularly and 4,216 (27.1%) men who received diagnostic PSA screenings. Regarding race, the table shows that the sample contained almost 92 percent Caucasians and only slightly greater than 8% African Americans. These percentages are similar to the percentages observed among men within the prostate cancer analysis where the larger sample size of 72,777 men approximated 90 percent and 10 percent respectively.

Table 33. Summary Count for Group and Race: Non-Cancer Group.

Statistics for sPSA					
N	Valid	15,557			
	Missing	0			
sPSA					
		Count	Percent	Valid Percent	Cumulative Percent
Valid	dPSA	4,216	27.1	27.1	27.1
	sPSA	11,341	72.9	72.9	100
	Total	15,557	100	100	
Statistics for Race					
N	Valid	15,557			
	Missing	0			
Race					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Cauc.	14,276	91.8	91.8	91.8
	AA	1,281	8.2	8.2	100

Table 36 illustrates the percentage of men for screening and race by each comorbid condition. Interestingly, it is noted that screened men and non-screened men were evenly proportioned on each comorbid condition with similar results appearing for race. As seen in the table, a majority of men within this non-cancer sample do not have any of the comorbid conditions (see Table 36).

An analysis of variance (ANOVA) between the screened and non-screened men for the socioeconomic variables (SES) (Census 2000) demonstrated statistically

Table 34. Summary Percent for Screened Men and Race by Comorbid Condition: Non-Cancer Group.

Comorbid Condition		Screened		Race	
		No	Yes	Caus.	AA
		%	%	%	%
Myocardial Infarction	No	94.4	93.4	93.6	94.9
	Yes	5.6	6.6	6.4	5.1
Old Myocardial Infarction	No	91.4	90.7	90.7	92.5
	Yes	8.6	9.3	9.3	7.5
CHF	No	86.6	87.9	87.9	84.2
	Yes	13.4	12.1	12.1	15.8
Peripheral Vascular Ds.	No	94.5	93.8	95.0	93.4
	Yes	5.5	6.2	6.0	6.6
Cerebro Vascular Ds.	No	87.4	87.2	87.4	85.9
	Yes	12.6	12.8	12.6	14.1
COPD	No	79.6	80.7	80.4	80.3
	Yes	20.4	19.3	19.6	19.7
Dementia	No	98.0	98.4	98.4	96.7
	Yes	2.0	1.6	1.6	3.3
Paralysis	No	96.6	97.3	97.3	94.7
	Yes	3.4	2.7	2.7	5.3
Diabetes	No	82.4	82.3	82.6	78.5
	Yes	17.6	17.7	17.4	21.5
Diabetes Sequelae	No	95.5	96.3	96.3	93.4
	Yes	4.5	3.7	3.7	6.6
Chronic Renal Failure	No	97.5	98.4	98.2	96.7
	Yes	2.5	1.6	1.8	3.3
Rheumatologic Process	No	99.0	98.7	98.7	99.1
	Yes	1.0	1.3	1.3	0.9

significant differences in the distribution for men never completing high school (p=.017) and those having only some college education (p=.002). Regarding race, the ANOVA of

Table 37 illustrates that there were statistical significant differences for all SES variables with the exception of those who graduated from high school (p=0.103).

Table 35. Analysis of Variance for Screening and Race on Socioeconomic Variables: Non-Cancer Group (Census Tract 2000).

ANOVA						
sPSA		Sum of Squares	Df	Mean Square	F	Sig.
NonHighSchoolGrad	Between Groups	562.6	1	562.6	5.65	.017
HighSchool	Between Groups	116.0	1	116.0	2.08	.149
SomeCollege	Between Groups	384.1	1	384.1	9.36	.002
College4yrs	Between Groups	194.2	1	194.2	1.35	.244
Median Income	Between Groups	354,524,101.3	1	354,524,101.3	1.25	.263
Race		Sum of Squares	Df	Mean Square	F	Sig.
NonHighSchoolGrad	Between Groups	25946.240	1	25946.240	265.18	.000
HighSchool	Between Groups	147.774	1	147.774	2.65	.103
SomeCollege	Between Groups	2829.700	1	2829.700	69.22	.000
College4yrs	Between Groups	14927.773	1	14927.773	105.03	.000
Median Income	Between Groups	35393920742.2	1	35393920742.2	126.023	.000

Statistical Modeling

Logistic and Cox Regression: Before Propensity Analysis

Table 38 lists select summary statistics from the multivariate logistic and Cox regression models for the non-cancer group without a propensity analysis applied. Complete output tables for both models are listed in Appendix L. Table 38 shows statistically significant differences in mortality for both the logistic and Cox regression models for screening and race. For example, the logistic model reported a greater overall mortality rate for non-screened men being approximately 29% more likely to die than screened men (OR 0.775, $\beta = -0.255$, $p<.0001$) and that African American men had a higher overall mortality rate with an odds ratio of 1.42 ($p<.0001$). Because this is a group of men without cancer, an explanation could be that men who chose screening were healthier and/or there is a survival benefit associated with early detection methods such as screening.

Although the Cox regression model showed greater overall mortality for screened men, the difference trended only slightly greater with an odds ratio of nearly one and a direction also close to equal as indicated by a near zero slope in the beta coefficient (OR 1.09, $\beta = .085$, $p=.002$). Regarding race, African American and Caucasian men also trended toward being equally likely to die with a similar odds ratio of 1.09 and $p=.046$ (see Table 38).

The Propensity Analysis

The p-scores for the men without prostate cancer were calculated first followed by the creation of a matched pair data set. Finally, the newly formed data set was evaluated

Table 36. Select Outputs from Logistic and Cox Regression Models: Non- Cancer Group Before Propensity Analysis.

Logistic Regression Case Processing Summary						
Unweighted Cases[a]		N	Percent			
Selected Cases	Included in Analysis	15,557	100			
	Missing Cases	0	0			
	Total	15,557	100			
Unselected Cases		0	0			
Total		15,557	100			
a. If weight is in effect, see classification table for the total number of cases.						
Cox Regression Case Processing Summary						
		N	Percent			
Cases available in analysis	Event[a]	6,754	43.40%			
	Censored	8,803	56.60%			
	Total	15,557	100.00%			
Cases dropped	Cases with missing values	0	0.00%			
	Cases with negative time	0	0.00%			
	Censored cases before the	0	0.00%			
	Total	0	0.00%			
Total		15,557	100.00%			
a. Dependent Variable: survival months						
Categorical Variables Codings both Logistic and Cox Regression						
		Frequency	Parameter coding			
			-1	-2	-3	-4
Age category	66-69 yrs.	750	0	0	0	0
	70-74 yrs.	2074	1	0	0	0
	75-79 yrs.	2873	0	1	0	0
	80-84 yrs.	5920	0	0	1	0
	85+ yrs.	3940	0	0	0	1
Race	1 Cauc.	14276	0			
	2 AA	1281	1			
Regression Outputs for Screening and African American Men: Non Cancer Group: Before Propensity Analysis						
	B	**S.E.**	**Wald**	**Df**	**Sig.**	**Exp(B)**
Logistic Model						
Being screened	-0.255	0.04	40.118	1	0	0.775
Being African American	0.352	0.066	28.187	1	0	1.422
Cox Regression Model						
Being Screened	0.085	0.028	9.395	1	0.002	1.089
Being African American	0.09	0.045	3.964	1	0.046	1.094

using logistic regression and conditional Cox regression. Before formal analysis, it was again helpful to examine how well the propensity scores overlapped or how well the two screening groups were balanced and matched. From the sample selection of 15,557 men of the non-cancer group, a final matched data set containing 8,426 men or 4,213 almost perfectly matched pairs was achieved. As seen in Figure 10, a plot of the propensity scores illustrates balance between groups. The dark thick line is the screened group (sPSA) and the light grey solid line overlays exactly on top and represents the non-screened group (dPSA).

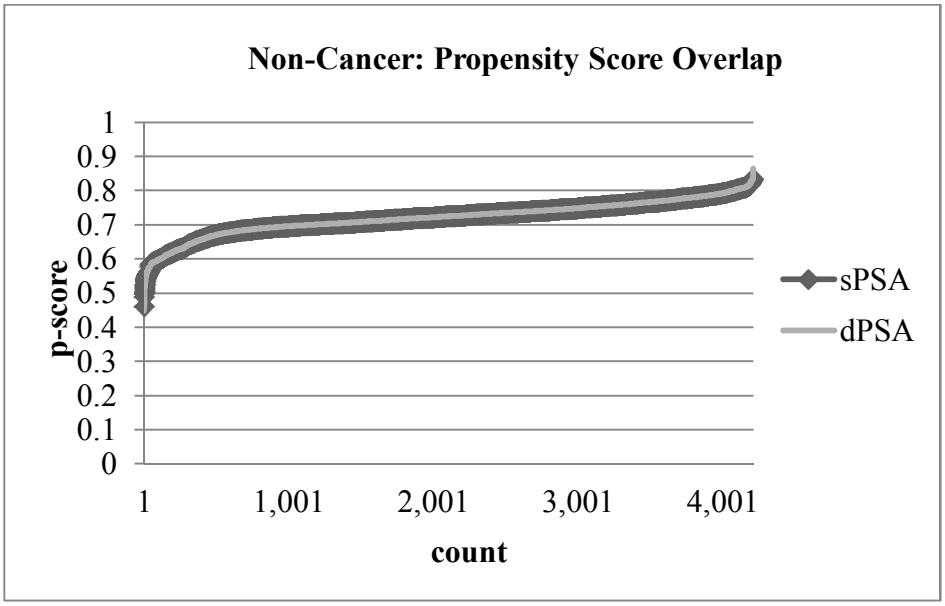

Figure 7. Plot of p-scores for sPSA and dPSA Groups: Non-Cancer Group after Propensity Analysis.

The same qualitative restrictions applied to the non-cancer group as did for the men with prostate cancer, namely, the absolute standardized differences of ±10 percent for before and after matching and the self-imposed absolute differences in p-scores of ±5 percent. Table 39 lists the absolute standardized differences. The table

Table 39. Variable Characterization of Significance and Percent Absolute Standardized Differences for Before and After Matching: Non-Cancer Group.

Having a Screening PSA test	**Before Match**		**After Match**	
	p-value	**Abs. Std. Diff (%)**	**p-value**	**Abs. Std. Diff (%)**
Race	<0.0001	45	0.447	0.02
Age	-	-	-	-
66-69 yrs.	<0.0001	1.41	.02	4.0
70-74 yrs.	<0.0001	5.9	.237	4.4
75-79 yrs.	<0.0001	3.9	.06	4.8
80-84 yrs.	<0.0001	12.7	.015	10
85+ yrs.	<0.0001	22	.004	4.3
Social Economic Variables	-	-	-	-
non-high school graduate	.370	0.70	.154	2.8
high school graduate	.388	2.6	.226	0.8
some college	.696	5.7	.652	5.5
4 yrs. College	.912	2.1	.244	0.26
median income	.007	2.1	.402	0.5
Comorbid Conditions	-	-	-	-
previous myocardial infarct	.874	4.4	0.88	3.2
myocardial infarct	.094	3.0	.954	2.4
CHF	.000	5.0	.838	1.7
peripheral vascular disease	.000	3.2	.840	0.13
cerebrovascular disease	.000	0.50	.980	4.1
COPD	.000	4.0	.793	0.30
Dementia	.000	3.3	1.000	0.51
Paralysis	.670	4.3	.815	0.57
Diabetes	.000	0.24	.035	0.57
diabetes with sequelae	.000	4.0	.768	1.77
chronic renal failure	.004	6.3	.838	0.49
rheumatologic process	.141	2.6	.505	3.5

shows only slight differences in before and after matching which could possibly indicate that this non-cancer group is healthier than what was observed in the cancer group.

Figure 11 is a plot of the absolute standardized differences for the **before** and **after** matching of pairs of the non-cancer group. As seen in the graph, the majority of covariates were unremarkable for the **before** match and remained nearly unchanged for the **after** match pairs.

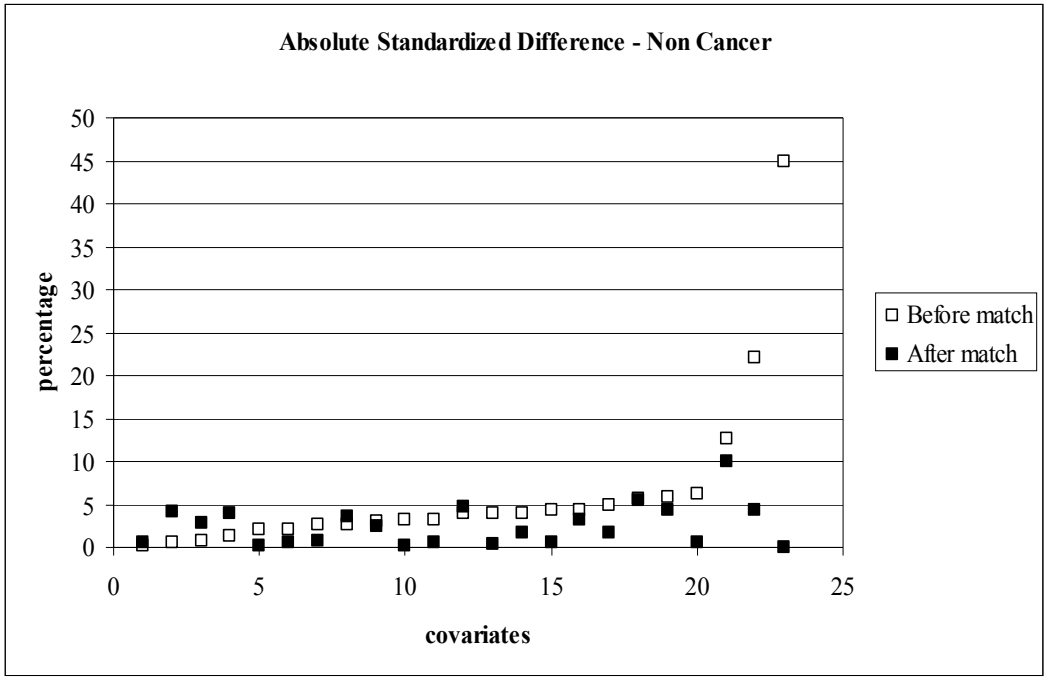

Figure 8. Absolute Standardized Differences for before and after Matching: Non-Cancer Group Analysis.

The last three data points for the **before** match are shown as white boxes and represent the largest differences for the age category of men between the ages of 80-84 years (12.7%), men over 85 years old (22%), and race (45%). These same three data points became more balanced after the match as shown with black boxes at 10%, 4.3%, and 0.02% respectively (see Figure 11).

Logistic and Cox Regression: After Propensity Analysis

After completing the propensity analysis and reviewing balance and overlap of variables modeling was performed for the non-cancer group. Select outputs from the logistic and conditional Cox regression models for the non-cancer group with a propensity analysis are shown below. Complete output results from both models are listed in Appendix M. Note that of the available cases included (8,426) there were no missing cases with 3,728 men censored (44.2%) leaving 4,698 (55.8%) men available for the analysis. Overall model resulted in correctly predicting 68.2 percent of the deaths (see Table 40).

The direction and significance for having a screening PSA test and being African American for the non-cancer group is shown below. Interestingly, when evaluating this group of men, the logistic regression model reported statistically significant differences in overall mortality for screened men and of African American race ($p = 0.00$ and $p = 0.00$) while the conditional Cox model resulted in no significant differences in mortality and screened men and being African American ($p = 0.447$ and $p = 0.832$). In particular, the negative beta coefficient (slope) from the logistic model indicated that non-screened men were more likely to die than screened men (OR 1.32) whereas the Cox model resulted in no differences. Regarding race, the logistic model indicated that African American men were more likely to die than Caucasian men (OR 1.45) with the Cox model showing no differences in mortality between races. These differences in statistical methods may indicate that a Cox regression approach, with its ability to censor on time-to-event terms as well as accounting for matched pairings through stratification, may be more robust and

Table 40. Select Outputs from Logistic and Cox Regression Models: Non-Cancer Group after Propensity Analysis.

Logistic Regression Case Processing Summary			
Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	8,426	100
	Missing Cases	0	0
	Total	8,426	100
Unselected Cases		0	0
Total		8,426	100
a. If weight is in effect, see classification table for the total number of cases.			

Conditional Cox Regression Case Processing Summary			
		N	Percent
Cases available in	Event[a]	4,010	47.60%
	Censored	688	8.20%
	Total	4,698	55.80%
Cases dropped	Cases with missing values	0	0.00%
	Cases with negative time	0	0.00%
	Censored cases before the earliest event in a stratum	3,728	44.20%
	Total	3,728	44.20%
Total		8,426	100.00%
a. Dependent Variable: survtimemonths			

Logistic Regression Omnibus Tests of Model				
		Chi-square	df	Sig.
Step 1	Step	1698.668	23	0
	Block	1698.668	23	0
	Model	1698.668	23	0

Model Summary			
Step	-2 Log likelihood	Cox & Snell R^2	Nagelkerke R^2
1	9962.678[a]	0.183	0.244

Classification					
	Observed		Predicted		
			Mortality		Percent Correct
			0	1	
Step 1	mortality	0	3295	1121	74.6
		1	1555	2455	61.2
	Overall Percentage				68.2

a. The cut value is .5

therefore, confirming it has a preferred statistical method for matched paired data sets as suggested by Luo, Gardiner & Bradley (2009) (see Table 41). Moreover, Cox regression modeling together with a propensity analysis and its ability to create equality through eliminating observed selection bias, may strengthen the external validity of retrospective observational studies.

Table 37. Model Output from Logistic and Cox Regression for Being Screened and African American: Non-Cancer Group after Propensity Analysis.

Regression Outputs for Screening and African American Men: Non-Cancer Propensity Analysis						
	B	**S.E.**	**Wald**	**Df**	**Sig.**	**Exp(B)**
Logistic Model						
Being screened	-.281	.049	33.464	1	.000	.755
Being African American	.371	.080	21.524	1	.000	1.449
Cox Regression Model						
Being Screened	-.048	.064	.578	1	.447	.953
Being African American	1.068	5.038	.045	1	.832	2.911

PSA Utilization Rates: Prostate Cancer Group

The final analysis of this study included examining the number of PSA tests and utilization rates among race for the group of men with prostate cancer (H_3) and then repeated for the group of men without prostate cancer (H_4). The number of PSA tests and utilization rates among race for the men with prostate cancer and for the total sample population of 322,822 men who had PSA tests recorded are shown in panels A and B of Figure 12, whether for screening purposes or for opportunistic reasons. Figure 12 shows that throughout the study period, Caucasian men tended to have more PSA tests each year with a maximum of over 53,000 occurring in 1993 compared to only 4,867 PSA tests for African American men that same year (panel A). However in looking at PSA utilization rates for the period (panel B), there were no significant differences among race (F-Test,

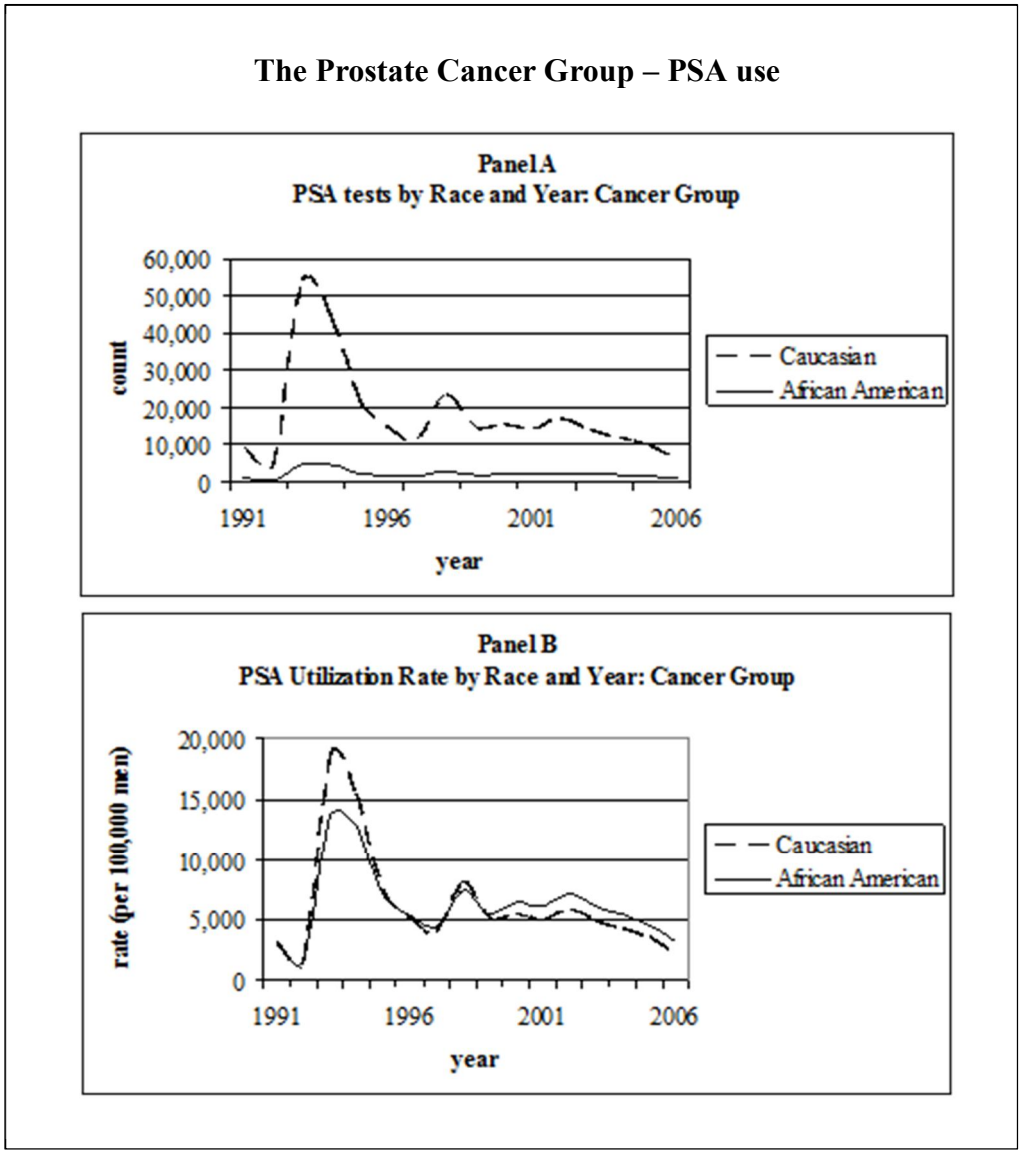

Figure 9. PSA count (panel A) and Utilization Rate (panel B) by Race and Year: Prostate Cancer Group.

one-tailed probability p=0.175). After 1993, it appears that for both Caucasian and African American men the number and rates tended to decline. In fact, the graph shows that after 1996, African American men tended to maintain a higher utilization rate than did Caucasian men.

When examining PSA utilization rates for the prostate cancer group, it was decided to also review the number of cases **diagnosed** as well as the **diagnosis rate** for the sample population. Figure 13 is a plot of the number of diagnoses by race and year (panel A) and the diagnosis rate by race and year (panel B). Panel A of Figure13 shows the number of diagnosis rising for Caucasian men until 1993 where it begins to decline slowly for seven years and then sharply rises again in 2000. This trend is followed by a slow decline throughout the remaining study period and ending in 2006. The number of diagnosis for African American men appears to have remained steady and then slowly rises around the year 2000 through 2006 (panel A). Panel B of Figure 13 shows similar trends for the diagnosis rate of both races throughout the study period and resulted in no statistically significant differences among the rates (F-Test, one-tailed probability $p=0.689$) (panel B). Interestingly, African American men experienced a higher diagnosis rate beginning in 1993 that coincided with a higher PSA utilization rate from 1995 forward. These trends lasted throughout the study period for African American men (see Figure 13, panel B).

PSA Utilization Rates: Non Cancer Group

In reviewing the numbers of PSA tests performed for the non-cancer group by race and year, a dramatic increase occurred from 1990 until around 1994 for Caucasians with only minimal increases in numbers for African Americans. The time period from 1997 through 2005 remained relatively unchanged for both races. The non-cancer group PSA utilization rates were similar for both Caucasian and African American men throughout the study period of 1992 through 2005. The data resulted in no statistically

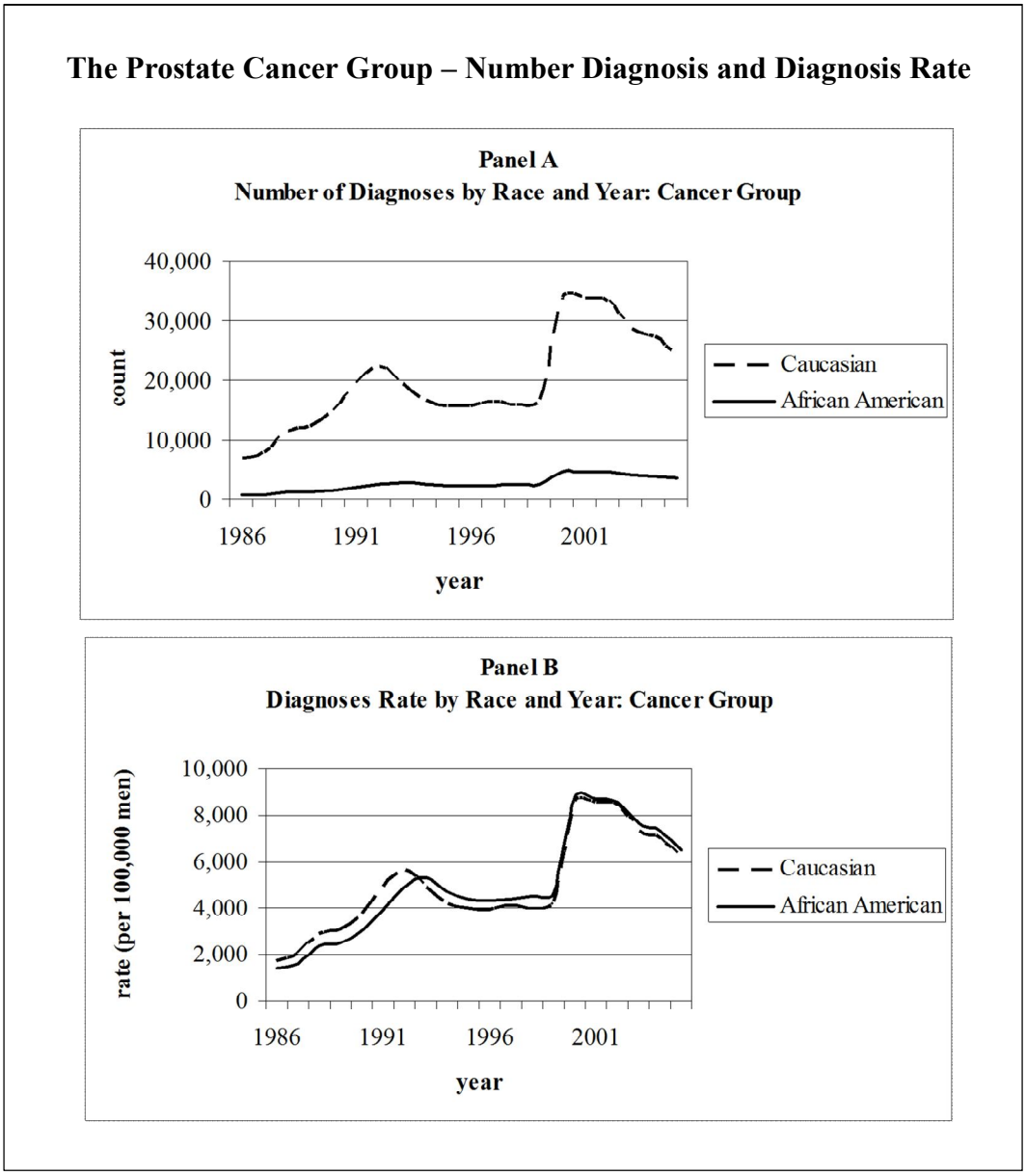

Figure 10. Number of Diagnosis (panel A) and Diagnosis Rate (panel B) by Race and Year: Prostate Cancer Group.

significant differences in the distributions of PSA utilization rates among race for the non-cancer group (F-Test, one-tailed probability p=0.466). In Figure 14, panel A shows

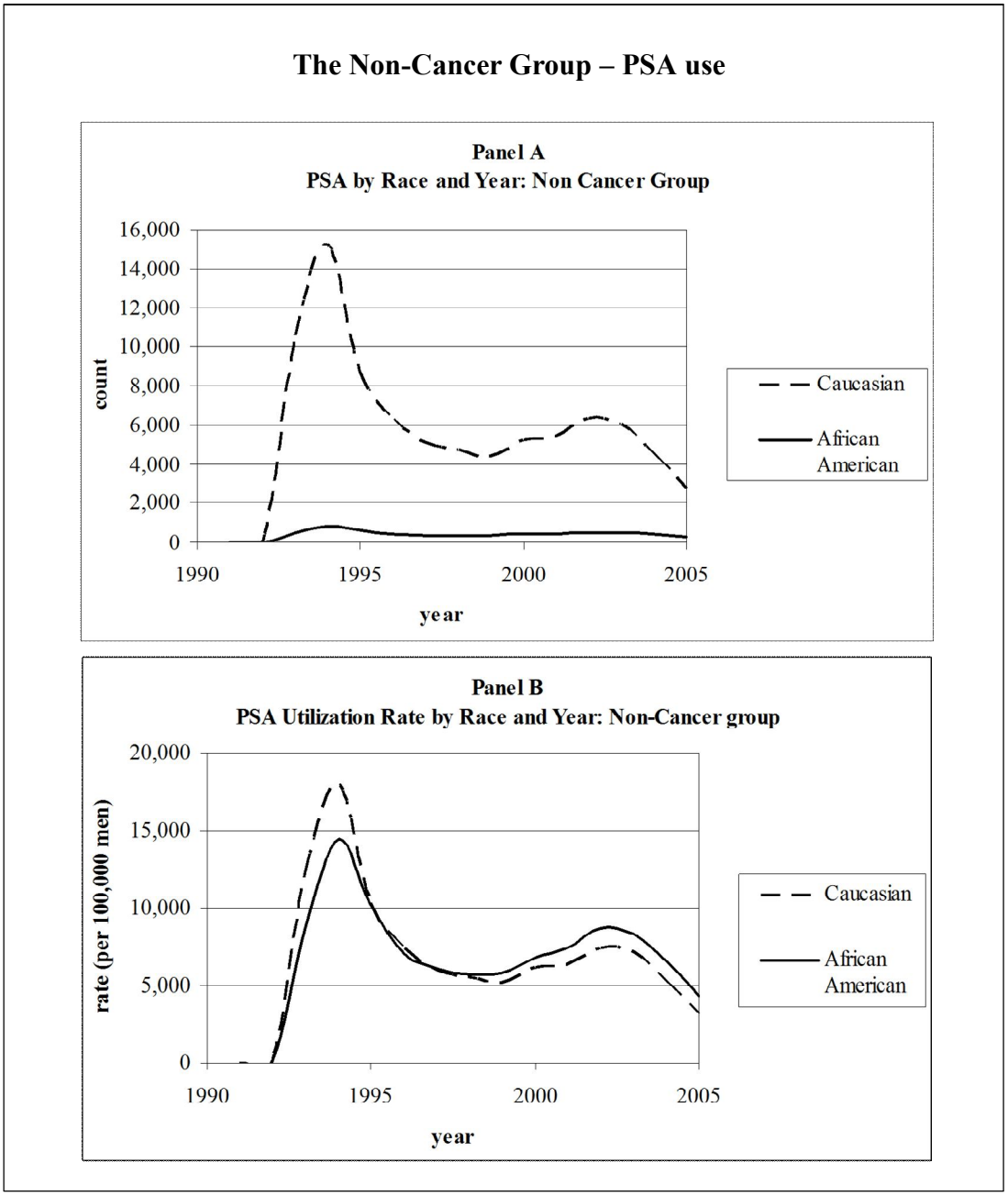

Figure 11. PSA Count (panel A) and PSA Utilization Rate (panel B) by Race and Year: Non-Cancer Group.

the numbers of PSA tests by race and year with panel B showing the PSA utilization rates among race by year for the non-cancer group (see Figure 14).

CHAPTER 5: DISCUSSION

The results provided in Chapter 4 demonstrate similar findings reported by other researchers who have used a propensity analysis for health services research studies in that, adjusting for a man's probability of receiving treatment based on a subset of observed covariates that almost exactly match those of another man should, theoretically, eliminate selection bias and remove differences between groups making them more equal thereby improving statistical inferences. Reduction in bias for equally matched groups would then render outcomes data more reliable and meaningful to large population-based retrospective observational analyses.

The current study used a propensity analysis adjustment for reducing selection bias and for balancing covariate distributions among race for a group of men with prostate cancer and a separate analysis in a group of men without cancer. It is suggested that balance across observed covariates is achieved through sufficient overlapping of p-scores and is noted by p-value changes from statistically significant to non-significant, by reduction in percent absolute standardized differences of less than 10%, and by plots of overlapping p-scores and/or the absolute standardized differences for both before and after application of the propensity analysis (Rubin 2002, D'Agostino 1998, Luellen 2005). Results in Chapter 4 of before and after comparisons, plots of p-scores overlap, and plots of absolute standardized differences demonstrated balance and equality of base-

line characteristics of comparison groups after applying a propensity score adjustment. These results demonstrate that this observational was sufficiently designed and are therefore believed to have strengthened the traditional regression modeling that occurred afterwards.

This project demonstrated that disparate mortality among Caucasians and African Americans with prostate cancer did not exist for this study population when using a propensity analysis for eliminating differences among groups. Comparisons were made of models from multivariate logistic regression and Cox regression for the full sample group with and without a propensity analysis, comparisons were evaluated for the data set when stratified into five quintiles, and comparisons were examined with the data set stratified by age. A summary table of the comparisons is presented below. Panel A shows that the multivariate logistic models for both before and after propensity adjustments for screening effects on mortality resulted in statistically significant differences (p=.001 and p=.007). This could be supportive of a screening protective effect on mortality trending toward a survival benefit for early detection. However, it may also represent a weakness of logistic regression's lack of censoring on time-to-event and its lack of accountability for matched paired data.

Results from the Cox regression model (panel A) demonstrated something vastly different than the logistic model illustrating no statistically significant differences in screening effects on mortality from both the before and after propensity score adjustment (p=.256 and p=.993). These results indicate that censoring for survival data on closely matched pairs using a Cox regression model could influence outcomes that lead to the

assumption that no survival benefit exists when screening for the early detection of prostate cancer (see Table 42).

Regarding whether differences exist among race and mortality, Table 42 panel A shows that before propensity score adjustments were applied, both the logistic and Cox regression models resulted in statistically significant differences for this sample population at p=.015 and p=.056 respectively, although the Cox model trended toward no difference among race and overall mortality at p=.056. In contrast, significance was lost once applying propensity score adjustments to both models for race and mortality (p=.559 and p=.081).

In looking at the results for the data sets when stratified into quintiles and age quartiles, Table 42 panel B shows for both regression models that for all five quintiles and the four age quartiles, no statistically significant differences exist among screened men and race on overall mortality with the exception of quintile 3, where significant differences were noted for only being screened (p=.004). This may be explained because p-scores of the third quintile may represent men who are less decisive or who may procrastinate about health behavior decision making and not communicate well with their physicians. Therefore, they may be men who show significant differences as a result of hidden or unobserved biases that go unaccounted for. In addition, quintile five resulted in constants or very high values for race and mortality which is again, believed to be the result of an under represented sample of African Americans among quintile five as described earlier (see Table 42 panel B).

Table 38. Model Summary Outputs: Compilation of Before and After Propensity Adjustment: Prostate Cancer Group.

Panel A	**Full Data Set**			
	Before Propensity (p-value)		**After Propensity (p-value)**	
	Logistic	**Cox**	**Logistic**	**Cox**
sPSA	0.001	0.256	0.007	0.993
AA	0.015	0.056	0.559	0.081
Panel B	**Quintile**	Being screened	0.068	0.919
	Q1	Being African American	0.353	0.493
	Q2	Being screened	0.432	0.355
		Being African American	0.515	0.976
	Q3	Being screened	0.004*	0.469
		Being African American	0.142	0.964
	Q4	Being screened	0.599	0.468
		Being African American	0.611	0.891
	Q5	Being screened	0.549	0.441
		Being African American	0.999	*
Age Qtr.1	66-69yrs	Being screened	0.565	1
		Being African American	0.508	1
Age Qtr. 2	70-74yrs	Being screened	0.432	0.829
		Being African American	0.055	0.209
Age Qtr. 3	75-79yrs	Being screened	0.225	0.247
		Being African American	0.554	0.32
Age Qtr. 4	over 80yrs	Being screened	0.741	1
		Being African American	0.898	1

Despite these few shortcomings, it is believed that enough data support the first hypothesis (H_1); therefore, the first hypothesis is accepted in favor of the null, that there were no statistically significant differences in mortality among race in men with prostate cancer for this sample population. Further support for accepting hypothesis one (H_1) is seen in Table 43. The table compares cancer-specific mortality rates between Caucasians and African Americans as a population calculated for both before and after a propensity

Table 39. Study Population: Crude Unadjusted and Age-Adjusted Mortality by Race for Models Before and After Propensity Analysis: Prostate Cancer Group.

Crude and Age-Adjusted Mortality for Race (per 100,000 men)		
African American: Caucasian	No Propensity	Propensity
Crude Unadjusted Mortality	1.23	1.04
66-69 yrs.	1.43	1.13
70-74 yrs.	1.23	0.96
75-79 yrs.	1.21	0.95
80-84 yrs.	1.16	0.99
85+ yrs.	1.32	1.03

analysis was applied. It shows crude unadjusted mortality for the entire study population and also for age-adjusted mortality by the ratio of African Americans to Caucasians. For example, the study sample population resulted in African American men having a 1.23 times greater mortality rate than Caucasian men before the propensity adjustment and nearly equal mortality rates (1.04) after applying p-scores. Differences in age-adjusted mortality rates improved as well after applying a propensity score adjustment (see Table 43).

In addition, Figure 15 illustrates further support for accepting hypothesis one in showing cancer-specific mortality rates by race and year before and after p-score adjustment. It appears that after applying a propensity adjustment, slight improvements were observed between before and after mortality rates (see Figure 15). Other researchers have reported similar results. In particular, Tewari compared long-term survival and different treatments in men with advanced stage prostate cancer using propensity scores. Their conclusion was that propensity scores showed slight improvements over the

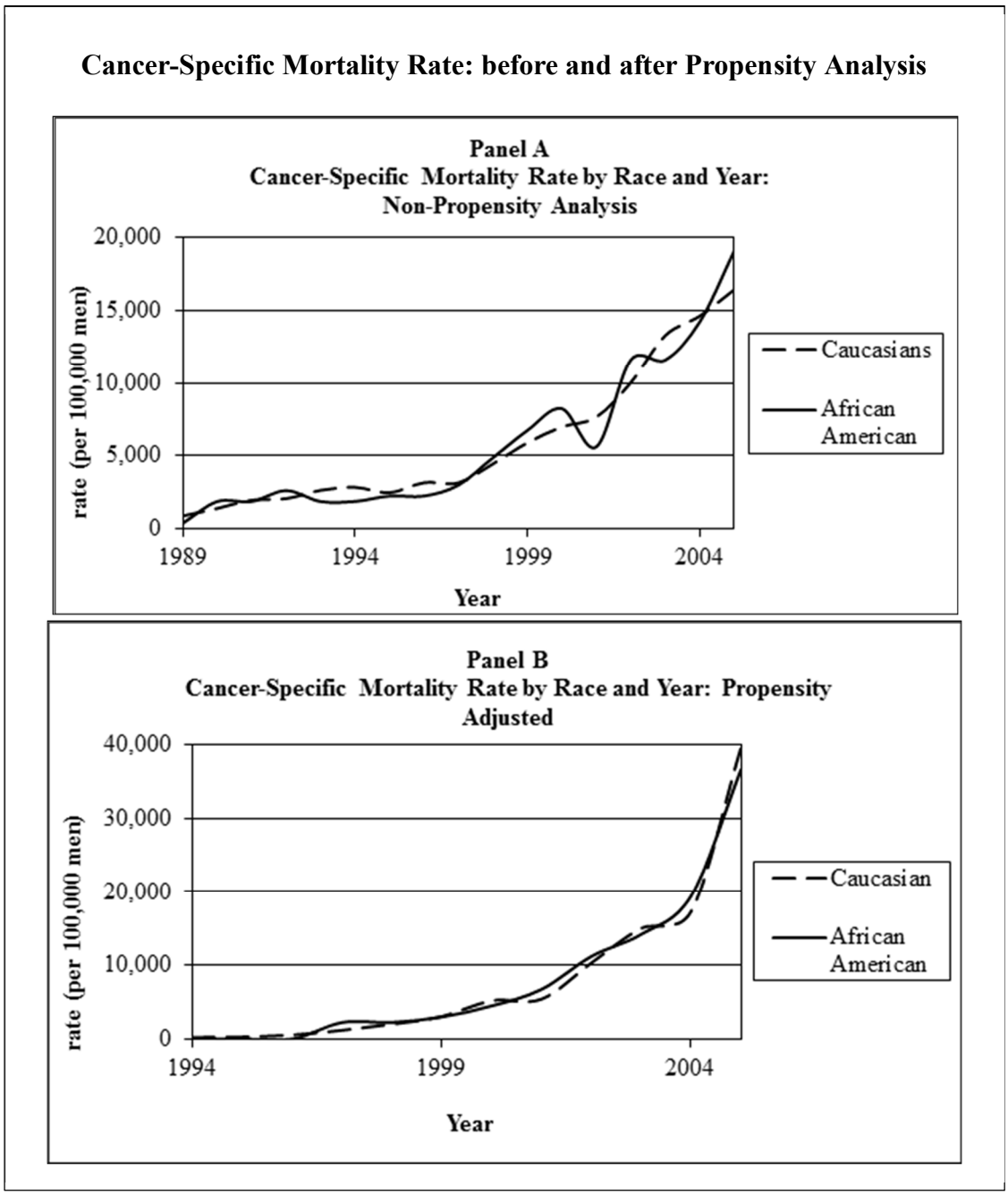

Figure 15. Cancer-Specific Mortality Rate by Race and Year: Before (panel A) and After (panel B) Propensity Analysis.

reported unadjusted rates and noted that using the propensity method was a strength of the study as it allowed the comparison of three treatment modalities when all observed covariates were matched and well balanced (Tewari et al., 2007).

Another study by Mitra et al. 2001 on breast cancer screenings found similar results using multiple logistic regression models to estimate the p-scores and placing women into five strata. The authors reported that before p-score adjustment, 9 out of 16 baseline covariates significantly differed between the two groups where after applying the p-score adjustment, all 16 covariates were balanced showing no significant differences. The authors noted that statistical significance was lost once adjusting with p-scores, therefore, allowing a more accurate assessment of the effectiveness for breast screening (Mitra, et al., 2001).

The results of Chapter 4 show mixed evidence regarding hypothesis 2 in that the logistic model demonstrated that statistically significant differences did exist between race and overall mortality among men within the non-cancer group while the Cox regression model resulted in no differences once the propensity analysis was applied. In reviewing Table 44, statistically significant differences remained unchanged between the before and after propensity analysis for being screened and African American from the logistic regression model ($p<0.0001$). However, the Cox regression model shows that significant differences were removed for screened men and being African American once p-scores were applied (see Table 44). Applying the propensity score adjustment appears to have improved the Cox regression model as no significant differences were noted in men who were screened and among race. African American men trended toward

Table 40. Model Results for Before and After Propensity Analysis: Non-Cancer Group.

	Before Propensity	After Propensity
	p-value	p-value
Logistic Model		
being screened	<.0001	<.0001
being African American	<.0001	<.0001
Cox Regression Model		
being screened	0.002	0.447
being African American	0.046	0.832

significant differences before applying p-score adjustments (p=.046) yet lost significance once they were applied (p=.832).

It may be intuitively tempting to reject hypothesis H_2 in favor of the alternative that statistically significant differences **do** exit in overall mortality rates among screened men and race when evaluating the logistic regression model for both with and without a p-score adjustment. This could be because logistic regression does not consider survival censorship for time to event nor does the model account for matched paired data and therefore, the results may underestimate the influence of unobserved covariates and other hidden conditions present thus influencing the model results toward statistically significant differences.

In contrast it is more compelling to accept hypothesis two (H_2) that no statistically significant differences exist among screened men and race in overall mortality when using a Cox regression and a propensity analysis. This is explained from knowing that the idea behind a screening program is to detect cancers early and therefore reduce mortality as a result. Because this second analysis was from a population of men who never had

prostate cancer or any other cancer, reason insists for an understanding that screening cannot affect mortality unless cancer is present and mortality is used as the end point measurement. Further, these men were clinically followed over a long time period on comorbid conditions and were nearly perfectly matched on observed covariates which could increase the predictive power that overall mortality would be no different among race. Therefore, hypothesis two is also accepted in favor of the null, that there were no statistically significant differences in overall racial mortality among men of this sample population.

In addressing hypothesis 3 and hypothesis 4 regarding PSA utilization for both the cancer and non-cancer groups, the results indicate no statistically significant differences in the distributions among race in men of the cancer group as well as among men without cancer (F-Test, one-tailed probability $p=0.466$ and $p=0.175$, respectively). Interestingly, African American men experienced a higher diagnosis rate beginning in 1993 that coincided with a higher PSA utilization rate from 1995 on through the end of the study period. Because of these findings, both hypothesis 3 and 4 are accepted in favor of the null, that no statistically significant differences in the distributions of PSA utilization rates existed between race for both the group of men with prostate cancer and among the group of men without cancer.

Strengths of Study

The current study utilized the most recent SEER population-based cancer registry data set compiled by the National Institute of Health sponsored by the National Cancer Institute merged with Medicare health care claims linked to patient demographic

information, initial PSA testing and diagnostic information, initial treatment, and long-term follow-up status of national cancer incidence and mortality rates making the data suitable for health services research (Warren, Klabunde, Schrag, Bach, & Riley, 2002).

The SEER Medicare linked database began collecting data in 1973 and now includes approximately 26% of the U.S. population. The SEER data are considered highly valid with quality and completeness studies performed yearly to ensure accuracy by holding the highest level of certification of quality as provided by the National American Association of Central Cancer Registries with a standard for completeness of data ascertained at 98% (Warren et al., 2002).

Use of a large national population-based data set along with a propensity analysis as part of the methodology is considered a strength of the current study (Rosenbaum & Rubin, 1983; Love, 2003; Grimes & Schulz, 2002). Further, use of a large national population-based data set provides sufficient amounts of patients for increased generalizability of results to the overall population. Use of such a large database allowed for extensive trimming of sample that still resulted in a sufficient final sample size and is considered a strength of this study.

Limitations of Study

As in most studies, limitations of the study include the lack of capturing claims from all services Medicare provides. For example, PSA screening provided by a community based screening program, services provided to a beneficiary by a Veteran's Administration facility, or services to a beneficiary who is employed and currently

covered by a health plan are not captured in the claims files and therefore, some men may have been excluded.

It has also been reported that using claims data to estimate prostate screening is limited (Freeman et al., 2002; Potosky et al., 1995; Legler et al., 1998; Cooper et al., 2001). For instance, claims data may lead to incomplete or missing information, as they are sometimes created only for purposes of payment and therefore reasons for having PSA tests (screening vs. diagnostic) nor PSA levels were not provided. In addition, this study did not include whether men had a DRE test along with their PSA blood test in which most screening programs would include both exams before recommending further clinical work up.

Further, large administrative databases are known to contain large amounts of selection bias that may threaten validity when using observational data for estimating outcomes. Potential explanations for undetected selection bias remaining, even with controlling, is lack of information for unobserved and unmeasured covariates as well as lack of information on self-reported health surveys often found in retrospective observational studies.

Other limitations may be the fact that this study only examined an elderly population of Medicare enrollees beginning at the age of 66 years old and did not consider younger men who are also susceptible to getting prostate cancer. Additionally, only cases of early stage disease of local/regional tumors were included. This restrictive age group and evaluation of only early stage disease could have limited the numbers of African American men in this study as it is known that African American men are

historically staged as late or advanced and can be found with prostate cancer at younger ages than Caucasian men. Finally, the study only examined men from two races. For these reasons results from this study can only be generalized to elderly men with similar early stage disease characteristics and among African Americans and Caucasians.

Areas for Future Research

The results of this study demonstrated that further work in health services is warranted and that it is feasible to apply a propensity analysis in observational retrospective research. Until results from randomized clinical trials are finalized, it may be beneficial to use retrospective observational studies of appropriate statistical methods and large population-based data sets as either surrogates for or complements to.

There are multitudes of agencies and programs working to end disparities in cancer morbidity and mortality through advocacy, research, and educational programs (ACS, 2008; Centers for Disease Control and Prevention, 2008; The **Patient Navigator** [P.L. 109-18], 2005). One theme of the ACS's 2015 challenge goals is to eliminate heath disparities within different segments of the U.S. population. The causes are complex with entangled variables likely from a combination of socioeconomic factors in work, income, education, and overall standard of living. In addition, economic and social barriers to prevention and early detection programs and the impact of racial and ethnic discrimination play a role. The ACS works alongside lawmakers at the local, state, and federal levels in order to create, change, and influence public policy that have a significant impact on reducing the cancer disparity in the United States. The ACS continues to fight for increased funding or to protect current funding to programs within

the Centers for Disease Control and Prevention (CDC) and health promotion. The effort extends into educational and screening programs targeted toward cancers that affect minorities, particularly African Americans. The **Patient Navigator** bill signed into law by President George W. Bush in 2005 provides grant funding to skilled workers who can provide culturally designed education and intervention programs for improving access to care, outcomes, and quality of life issues to underserved communities (ACS-AA, 2007/2008). The ACS has funded 76 studies allocating over 62 million dollars since 1999 to the poor and underprivileged with 42 percent of funding devoted to African Americans. Studies include early detection and prevention programs, treatment improvements, and psychosocial coping and supportive measures (ACS-AA, 2009/2010).

Prostate cancer screening with regard to when to begin, how often to repeat, and what the results tell physicians and patients continue to be topics for discussion at scientific seminars and medical meetings. Hopefully, this study will provoke new ideas and raise new questions that may someday lead to an actual finding of the effects that screening PSA tests have on mortality.

Conclusion

The results of this study are supportive of some research outcomes and contractive to others. Key findings of the study were that no significant differences exist in cancer-specific and overall mortality among race in men with prostate cancer and in men without prostate cancer. In addition and like the PLCO randomized clinical trial findings, no statistically significant survival benefit was noted for the PSA screening test. Further, no significant differences were found among both groups for PSA screening

utilizations throughout the study period. These results could help shape future best-practice guidelines and help guide public policy toward a more individualized race-based screening protocol providing physicians with new information about ways to communicate screening tests that may be best for their patients.

It is usually accepted that hope lies within randomized clinical trials for showing whether PSA screening for early detection and prevention can lead to reduced mortality rates. However, it may now be safe to believe that well-designed retrospective observational studies may serve as surrogates when time and economic resources are limited. Should factors be identified from either design showing differences exist between African American and Caucasian men regarding screening and mortality then new race-based public policy prevention mechanisms should be expanded and further examined.

Finally, it is believed that this study shows that Cox regression maybe an improved, more robust method for evaluating large population samples where censoring for survival is important and where matched pairs are utilized. Additionally, the results further suggest that applying a propensity analysis was helpful for this study. The two analyses together may play a role in future research. Further work in health services research using large population-based secondary data sets should be pursued incorporating Cox regression with survival time censoring, matched pairs, and a propensity analysis.

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APPENDICES

Appendix A

Logistic and Cox Regression: Non-Propensity Analysis

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	67307	92.5
	Missing Cases	5470	7.5
	Total	72777	100.0
Unselected Cases		0	.0
Total		72777	100.0

a. If weight is in effect, see classification table for the total number of cases.

Dependent Variable Encoding

Original Value	Internal Value
0	0
1	1

Categorical Variables Codings

			Parameter coding				
		Frequency	(1)	(2)	(3)	(4)	(5)
Marital Status	1	4127	.000	.000	.000	.000	.000
	2	49457	1.000	.000	.000	.000	.000
	3	233	.000	1.000	.000	.000	.000
	4	2466	.000	.000	1.000	.000	.000
	5	5012	.000	.000	.000	1.000	.000
	9	6012	.000	.000	.000	.000	1.000
Radiation	0	34404	.000	.000	.000	.000	
	1	18301	1.000	.000	.000	.000	
	2	9047	.000	1.000	.000	.000	
	4	4743	.000	.000	1.000	.000	

	9	812	.000	.000	.000	1.000
Age at Diagnosis	14	20559	.000	.000	.000	.000
Year	15	23646	1.000	.000	.000	.000
	16	15500	.000	1.000	.000	.000
	17	5920	.000	.000	1.000	.000
	18	1682	.000	.000	.000	1.000
Grade	1	4338	.000			
	2	62969	1.000			
SEER Race Recode	1	61110	.000			
	2	6197	1.000			

Block 0: Beginning Block

Classification Table[a,b]

			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 0	Mortality	0	64695	0	100.0
		1	2612	0	.0
	Overall Percentage				96.1

a. Constant is included in the model.
b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp (B)
Step 0	Constant	-3.210	.020	25862.871	1	.000	.040

Variables not in the Equation[a]

		Score	Df	Sig.
Variables	sPSA	220.711	1	.000
	Race	9.440	1	.002
	Age	451.441	4	.000
	Age(1)	36.059	1	.000
	Age(2)	46.911	1	.000
	Age(3)	133.970	1	.000
	Age(4)	179.288	1	.000

Grade	47.339	1	.000
HistStageCombinary	2130.418	1	.000
MarStatus	103.361	5	.000
MarStatus(1)	84.470	1	.000
MarStatus(2)	.106	1	.745
MarStatus(3)	.082	1	.774
MarStatus(4)	19.777	1	.000
MarStatus(5)	58.916	1	.000
Radiation	221.652	4	.000
Radiation(1)	5.190	1	.023
Radiation(2)	171.911	1	.000
Radiation(3)	24.183	1	.000
Radiation(4)	1.015	1	.314
RadSurgCombinary	127.107	1	.000
SurgCombinary	722.977	1	.000
Hormones	203.011	1	.000
PctNonHSGrad	4.898	1	.027
PctHSonly	4.746	1	.029
PctSomeColl	.000	1	.991
Pct4yrColl	6.952	1	.008
MedIncome	12.643	1	.000
MyoInfarc	.587	1	.443
OldMyoInfarc	9.516	1	.002
CHF	66.814	1	.000
PeriphVascDisDx	41.460	1	.000
CerebroVascDis	16.067	1	.000
COPD	23.668	1	.000
Dementia	158.872	1	.000
Paralysis	7.745	1	.005
Diabetes	21.596	1	.000
DiabetesSequelae	10.350	1	.001
ChronicRenalFail	16.698	1	.000
Rheum	5.886	1	.015

a. Residual Chi-Squares are not computed because of redundancies.

Block 1: Method = Enter

Omnibus Tests of Model Coefficients				
		Chi-square	Df	Sig.
Step 1	Step	2551.208	37	.000
	Block	2551.208	37	.000
	Model	2551.208	37	.000

Model Summary			
Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	19543.639[a]	.037	.133

a. Estimation terminated at iteration number 7 because parameter estimates changed by less than .001.

Hosmer and Lemeshow Test			
Step	Chi-square	Df	Sig.
1	29.104	8	.000

Classification Table[a]					
			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 1	Mortality	0	64680	15	100.0
		1	2552	60	2.3
	Overall Percentage				96.2

a. The cut value is .500

Variables in the Equation								
Variables	B	S.E.	Wald	Df	Sig.	Exp (B)	95% C.I. for EXP(B)	
							Lower	Upper
sPSA	-.159	.048	10.929	1	.001	.853	.776	.937
Race	.177	.073	5.869	1	.015	1.194	1.034	1.378
Age			577.90	4	.000			

Age(1)	.398	.059	45.168	1	.000	1.489	1.326	1.672
Age(2)	.966	.061	247.93	1	.000	2.628	2.331	2.964
Age(3)	1.353	.074	337.7	1	.000	3.870	3.350	4.471
Age(4)	1.795	.099	328.06	1	.000	6.019	4.957	7.310
Grade	.001	.073	.000	1	.994	1.001	.867	1.154
HistStage Combine	-1.697	.063	723.87	1	.000	.183	.162	.207
MarStatus			115.02	5	.000			
MarStatus(1)	-.373	.081	21.166	1	.000	.689	.588	.807
MarStatus(2)	-.161	.346	.217	1	.641	.851	.432	1.676
MarStatus(3)	-.115	.132	.749	1	.387	.892	.688	1.156
MarStatus(4)	-.233	.103	5.156	1	.023	.792	.648	.969
MarStatus(5)	.294	.097	9.209	1	.002	1.342	1.110	1.624
Radiation			56.364	4	.000			
Radiation(1)	.105	.052	4.002	1	.045	1.110	1.002	1.230
Radiation(2)	-.502	.098	26.241	1	.000	.605	.500	.734
Radiation(3)	-.056	.102	.299	1	.585	.946	.775	1.155
Radiation(4)	-.902	.210	18.421	1	.000	.406	.269	.612
RadSurgCombined	.256	.096	7.170	1	.007	1.291	1.071	1.557
SurgCombinary	.924	.050	338.11	1	.000	2.520	2.283	2.780
Hormones	.815	.064	160.59	1	.000	2.259	1.991	2.562
PctNonHSGrad	-.008	.017	.233	1	.630	.992	.959	1.026
PctHSonly	-.003	.017	.035	1	.852	.997	.963	1.031
PctSomeColl	-.011	.017	.375	1	.541	.989	.956	1.024
Pct4yrColl	-.009	.017	.240	1	.624	.992	.958	1.026
MedIncome	.000	.000	.136	1	.713	1.000	1.000	1.000
MyoInfarc	-.813	.767	1.124	1	.289	.443	.099	1.995
OldMyoInfarc	4.091	2.653	2.378	1	.123	59.816	.330	10841.5
CHF	.390	.120	10.463	1	.001	1.477	1.166	1.870
PeriphVascDis	.890	.321	7.694	1	.006	2.435	1.298	4.567
CerebroVascDis	-.102	.378	.073	1	.786	.903	.430	1.894
COPD	.084	.096	.752	1	.386	1.087	.900	1.313
Dementia	2.133	.305	48.878	1	.000	8.442	4.642	15.353
Paralysis	1.050	.817	1.653	1	.199	2.858	.577	14.169
Diabetes	.543	.316	2.943	1	.086	1.720	.926	3.198

DiabetesSequelae	.315	.354	.792	1	.374	1.370	.685	2.742
ChronicRenalFail	.327	.292	1.255	1	.263	1.387	.782	2.459
Rheum	1.346	2.033	.439	1	.508	3.843	.072	206.483
Constant	-1.958	1.733	1.276	1	.259	.141		

a. Variable(s) entered on step 1: sPSA, Race, Age, Grade, HistStageCombinary, MarStatus, Radiation, RadSurgCombinary, SurgCombinary, Hormones, PctNonHSGrad, PctHSonly, PctSomeColl, Pct4yrColl, MedIncome, MyoInfarc, OldMyoInfarc, CHF, PeriphVascDisDx, CerebroVascDis, COPD, Dementia, Paralysis, Diabetes, DiabetesSequelae, ChronicRenalFail, Rheum.

Cox Regression: Non-Propensity Analysis

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	2612	3.6%
	Censored	64695	88.9%
	Total	67307	92.5%
Cases dropped	Cases with missing values	5470	7.5%
	Cases with negative time	0	.0%
	Censored cases before the earliest event in a stratum	0	.0%
	Total	5470	7.5%
Total		72777	100.0%

a. Dependent Variable: Survival time recode (total # of months)

Categorical Variable Codings[b,c,d,e,f]

		Frequency	(1)	(2)	(3)	(4)	(5)
Age[a]	14	20559	0	0	0	0	
	15	23646	1	0	0	0	
	16	15500	0	1	0	0	
	17	5920	0	0	1	0	

	18	1682	0	0	0	1	
Grade[a]	1	4338	0				
	2	62969	1				
MarStatus[a]	1	4127	0	0	0	0	0
	2	49457	1	0	0	0	0
	3	233	0	1	0	0	0
	4	2466	0	0	1	0	0
	5	5012	0	0	0	1	0
	9	6012	0	0	0	0	1
Race[a]	1	61110	0				
	2	6197	1				
Radiation[a]	0	34404	0	0	0	0	
	1	18301	1	0	0	0	
	2	9047	0	1	0	0	
	4	4743	0	0	1	0	
	9	812	0	0	0	1	

a. Indicator Parameter Coding
b. Category variable: Age (Age at Diagnosis Year)
c. Category variable: Grade (Grade)
d. Category variable: MarStatus (Marital Status)
e. Category variable: Race (SEER Race Recode B)
f. Category variable: Radiation (Radiation)

Block 0: Beginning Block

Omnibus Tests of Model Coefficients
-2 Log Likelihood
52093.490

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]

	Overall (score)			Change From Previous Step			Change From Previous Block		
-2 Log Likelihood	Chi-square	Df	Sig.	Chi-square	Df	Sig.	Chi-square	df	Sig.
50706.859	1830.31	37	.000	1386.63	37	.000	1386.63	37	.000

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

	B	SE	Wald	Df	Sig.	Exp (B)	95.0% CI for Exp (B)	
							Lower	Upper
sPSA	-.053	.047	1.289	1	.256	.948	.865	1.039
Race	.134	.070	3.650	1	.056	1.144	.997	1.312
Age			672.203	4	.000			
Age(1)	.344	.057	36.587	1	.000	1.411	1.262	1.578
Age(2)	.899	.059	235.718	1	.000	2.456	2.190	2.755
Age(3)	1.337	.070	366.609	1	.000	3.808	3.321	4.366
Age(4)	1.898	.092	421.869	1	.000	6.674	5.568	7.999
Grade	.281	.068	17.101	1	.000	1.325	1.159	1.513
HistStageCombinary	-.415	.067	38.525	1	.000	.661	.579	.753
MarStatus			99.915	5	.000			
MarStatus(1)	-.367	.076	23.048	1	.000	.693	.597	.805
MarStatus(2)	.036	.325	.012	1	.913	1.036	.548	1.959
MarStatus(3)	-.052	.126	.169	1	.681	.950	.742	1.216
MarStatus(4)	-.226	.096	5.513	1	.019	.798	.661	.963
MarStatus(5)	.200	.091	4.772	1	.029	1.221	1.021	1.461
Radiation			47.810	4	.000			
Radiation(1)	-.185	.049	14.038	1	.000	.831	.754	.915
Radiation(2)	-.555	.096	33.560	1	.000	.574	.476	.693
Radiation(3)	-.386	.098	15.428	1	.000	.680	.561	.824
Radiation(4)	-.213	.204	1.093	1	.296	.808	.542	1.205
RadSurgCombinary	.531	.088	36.594	1	.000	1.700	1.431	2.019
SurgCombinary	-.283	.052	29.434	1	.000	.753	.680	.834
Hormones	.730	.059	152.076	1	.000	2.074	1.847	2.329

PctNonHSGrad	.001	.020	.001	1	.979	1.001	.962	1.041
PctHSonly	.003	.020	.028	1	.867	1.003	.965	1.044
PctSomeColl	-.010	.020	.251	1	.616	.990	.952	1.030
Pct4yrColl	-.006	.020	.092	1	.762	.994	.956	1.034
MedIncome	.000	.000	2.662	1	.103	1.000	1.000	1.000
MyoInfarc	-1.244	.723	2.956	1	.086	.288	.070	1.190
OldMyoInfarc	4.648	2.47	3.522	1	.061	104.368	.814	13383.93
CHF	.386	.110	12.443	1	.000	1.472	1.187	1.824
PeriphVascDis	.896	.293	9.338	1	.002	2.449	1.379	4.351
CerebroVascDis	-.080	.351	.052	1	.819	.923	.464	1.836
COPD	.035	.090	.150	1	.699	1.035	.868	1.235
Dementia	1.849	.239	59.818	1	.000	6.352	3.976	10.149
Paralysis	.627	.732	.734	1	.392	1.872	.446	7.854
Diabetes	.671	.294	5.199	1	.023	1.955	1.099	3.480
DiabetesSequelae	.324	.328	.974	1	.324	1.383	.727	2.631
ChronicRenalFail	.481	.266	3.273	1	.070	1.617	.961	2.723
Rheum	1.995	1.87	1.132	1	.287	7.350	.186	289.843

Appendix B

Logistic Regression: FM with Propensity Analysis

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	50,000	100.0
	Missing Cases	0	.0
	Total	50,000	100.0
Unselected Cases		0	.0
Total		50,000	100.0

a. If weight is in effect, see classification table for the total number of cases.

b. The variable Hormones is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

Dependent Variable Encoding

Original Value	Internal Value
0	0
1	1

Categorical Variables Codings

			Parameter coding				
		Frequency	(1)	(2)	(3)	(4)	(5)
Marital Status	1	3177	.000	.000	.000	.000	.000
	2	36007	1.000	.000	.000	.000	.000
	3	170	.000	1.000	.000	.000	.000
	4	1877	.000	.000	1.000	.000	.000
	5	3839	.000	.000	.000	1.000	.000
	9	4930	.000	.000	.000	.000	1.000
Age Group	14	15390	.000	.000	.000	.000	

	15	17268	1.000	.000	.000	.000
	16	11082	.000	1.000	.000	.000
	17	4856	.000	.000	1.000	.000
	18	1404	.000	.000	.000	1.000
Grade 1	1	3298	.000			
	2	46702	1.000			
SEER Race	1	45603	.000			
Recode B	2	4397	1.000			

Block 0: Beginning Block

Classification Table[a,b]

			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 0	Mortality	0	48,420	0	100.0
		1	1,580	0	.0
	Overall Percentage				96.8

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	Df	Sig.	Exp (B)
Step 0	Constant	-3.422	.026	17922.383	1	.000	.033

Variables not in the Equation[a]

		Score	df	Sig.
Variables	sPSA	4.834	1	.028
	Race(1)	.199	1	.655
	Age	317.368	4	.000
	Age(1)	22.218	1	.000
	Age(2)	61.884	1	.000
	Age(3)	83.037	1	.000
	Age(4)	90.969	1	.000
	Grade(1)	12.107	1	.001

HistStageCombinary	175.412	1	.000
MarStatus	99.868	5	.000
MarStatus(1)	68.013	1	.000
MarStatus(2)	.076	1	.783
MarStatus(3)	.002	1	.966
MarStatus(4)	5.619	1	.018
MarStatus(5)	81.400	1	.000
Radiation	46.106	1	.000
RadSurgCombinary	8.689	1	.003
SurgCombinary	132.255	1	.000
PctNonHSGrad	1.463	1	.226
PctHSonly	1.104	1	.293
PctSomeColl	.825	1	.364
Pct4yrColl	2.805	1	.094
MedIncome	.049	1	.824
MyoInfarc	.329	1	.566
OldMyoInfarc	.338	1	.561
CHF	7.314	1	.007
PeriphVascDisDx	3.894	1	.048
CerebroVascDis	2.229	1	.135
COPD	5.360	1	.021
Dementia	52.031	1	.000
Paralysis	1.624	1	.203
Diabetes	3.232	1	.072
DiabetesSequelae	1.844	1	.175
ChronicRenalFail	2.445	1	.118
Rheum	1.360	1	.244

a. Residual Chi-Squares are not computed because of redundancies.

Block 1: Method = Enter

Omnibus Tests of Model Coefficients

		Chi-square	Df	Sig.
Step 1	Step	713.126	33	.000
	Block	713.126	33	.000
	Model	713.126	33	.000

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	13312.942[a]	.014	.058

a. Estimation terminated at iteration number 7 because parameter estimates changed by less than .001.

Classification Table[a]

			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 1	Mortality	0	48419	1	100.0
		1	1577	3	.2
	Overall Percentage				96.8

a. The cut value is .500

Variables in the Equation

	B	S.E.	Wald	Df	Sig.	Exp (B)	95% C.I. for exp (B)	
							Lower	Upper
sPSA	-.140	.052	7.282	1	.007	.870	.786	.962
Race(1)	.058	.099	.342	1	.559	1.060	.872	1.287
Age			304.33	4	.000			
Age(1)	.386	.077	24.854	1	.000	1.471	1.264	1.712
Age(2)	.948	.078	146.35	1	.000	2.580	2.213	3.009
Age(3)	1.209	.092	174.23	1	.000	3.350	2.799	4.008
Age(4)	1.565	.122	165.15	1	.000	4.782	3.767	6.071
Grade(1)	-.082	.093	.766	1	.381	.922	.767	1.107
HistStageCombine	-1.484	.153	94.354	1	.000	.227	.168	.306
MarStatus			94.225	5	.000			
MarStatus(1)	-.321	.102	9.810	1	.002	.726	.594	.887
MarStatus(2)	.035	.430	.007	1	.934	1.036	.446	2.407
MarStatus(3)	-.060	.165	.131	1	.717	.942	.682	1.301
MarStatus(4)	-.192	.130	2.184	1	.139	.825	.640	1.065

MarStatus(5)	.381	.117	10.574	1	.001	1.463	1.163	1.840
Radiation	-.089	.021	18.632	1	.000	.915	.878	.952
RadSurgCombine	.237	.138	2.945	1	.086	1.268	.967	1.663
SurgCombinary	.734	.056	170.02	1	.000	2.084	1.867	2.328
PctNonHSGrad	-.023	.018	1.648	1	.199	.977	.943	1.012
PctHSonly	-.015	.018	.701	1	.402	.985	.950	1.021
PctSomeColl	-.025	.018	1.966	1	.161	.975	.941	1.010
Pct4yrColl	-.017	.018	.931	1	.335	.983	.948	1.018
MedIncome	.000	.000	.096	1	.756	1.000	1.000	1.000
MyoInfarc	-.099	.974	.010	1	.919	.906	.134	6.108
OldMyoInfarc	.375	3.767	.010	1	.921	1.455	.001	2342.6
CHF	.219	.181	1.469	1	.225	1.245	.874	1.774
PeriphVascDisDx	.433	.459	.888	1	.346	1.542	.627	3.792
CerebroVascDis	-.079	.500	.025	1	.874	.924	.347	2.461
COPD	.155	.123	1.591	1	.207	1.168	.918	1.487
Dementia	2.122	.446	22.627	1	.000	8.345	3.481	20.002
Paralysis	1.293	1.220	1.122	1	.290	3.642	.333	39.829
Diabetes	.400	.409	.957	1	.328	1.493	.669	3.329
DiabetesSequelae	.216	.476	.205	1	.651	1.240	.488	3.154
ChronicRenalFail	.460	.470	.958	1	.328	1.584	.631	3.977
Rheum	1.327	2.636	.253	1	.615	3.769	.021	660.83
Constant	-.462	1.800	.066	1	.797	.630		

a. Variable(s) entered on step 1: sPSA, Race, Age, Grade, HistStageCombinary, MarStatus, Radiation, RadSurgCombinary, SurgCombinary, PctNonHSGrad, PctHSonly, PctSomeColl, Pct4yrColl, MedIncome, MyoInfarc, OldMyoInfarc, CHF, PeriphVascDisDx, CerebroVascDis, COPD, Dementia, Paralysis, Diabetes, DiabetesSequelae, ChronicRenalFail, Rheum.

Cox Regression: FM with Propensity Analysis

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	1580	3.2%
	Censored	834	1.7%
	Total	2414	4.8%

Cases dropped	Cases with missing values	0	.0%
	Cases with negative time	0	.0%
	Censored cases before the earliest event in a stratum	47586	95.2%
	Total	47586	95.2%
Total		50000	100.0%

a. Dependent Variable: Survival time recode (total # of months)

Categorical Variable Codings[b,c,d,e]

		Frequency	(1)	(2)	(3)	(4)	(5)
Race[a]	1	45603	0				
	2	4397	1				
Age[a]	14	15390	0	0	0	0	
	15	17268	1	0	0	0	
	16	11082	0	1	0	0	
	17	4856	0	0	1	0	
	18	1404	0	0	0	1	
Grade[a]	1	3298	0				
	2	46702	1				
MarStatus[a]	1	3177	0	0	0	0	0
	2	36007	1	0	0	0	0
	3	170	0	1	0	0	0
	4	1877	0	0	1	0	0
	5	3839	0	0	0	1	0
	9	4930	0	0	0	0	1

a. Indicator Parameter Coding

b. Category variable: Race (SEER Race Recode B)

c. Category variable: Age (Age at Diagnosis Year 1)

d. Category variable: Grade (Grade 1)

e. Category variable: MarStatus (Marital Status)

Block 0: Beginning Block

Omnibus Tests of Model Coefficients
-2 Log Likelihood
1186.668

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]

	Overall (score)			Change From Previous Step			Change From Previous Block		
-2 Log Likelihood	Chi-square	Df	Sig.	Chi-square	Df	Sig.	Chi-square	df	Sig.
1006.454	159.521	31	.000	180.214	31	.000	180.214	31	.000

a. Beginning Block Number 1. Method = Enter

Variables in the Equation[b]

	B	SE	Wald	df	Sig.	Exp (B)	95.0% CI for Exp (B)	
							Lower	Upper
sPSA	-.001	.078	.000	1	.993	.999	.857	1.165
Race	-.644	.369	3.040	1	.081	.525	.255	1.083
Age			57.235	4	.000			
Age(1)	.944	.401	5.545	1	.019	2.570	1.172	5.640
Age(2)	1.448	.419	11.926	1	.001	4.255	1.870	9.678
Age(3)	1.707	.375	20.769	1	.000	5.512	2.645	11.486
Age(4)	2.309	.398	33.655	1	.000	10.065	4.613	21.960
Grade	.366	.228	2.576	1	.108	1.441	.922	2.252
HistStageCombine			.	0[a]	.			
MarStatus			14.107	5	.015			
MarStatus(1)	-.048	.273	.032	1	.859	.953	.558	1.627
MarStatus(2)	1.032	.956	1.167	1	.280	2.808	.431	18.278

MarStatus(3)	.192	.347	.308	1	.579	1.212	.614	2.393
MarStatus(4)	.107	.314	.117	1	.732	1.113	.602	2.059
MarStatus(5)	.597	.283	4.438	1	.035	1.816	1.042	3.165
Radiation	-.142	.044	10.485	1	.001	.868	.797	.946
RadSurgCombinar	.942	.302	9.766	1	.002	2.566	1.421	4.634
SurgCombinary	-1.20	.311	15.116	1	.000	.299	.163	.549
Hormones			.	0[a]	.			
PctNonHSGrad	-.006	.094	.003	1	.953	.994	.827	1.196
PctHSonly	-.011	.095	.014	1	.905	.989	.821	1.191
PctSomeColl	-.003	.094	.001	1	.974	.997	.829	1.198
Pct4yrColl	.002	.094	.000	1	.983	1.002	.833	1.206
MedIncome	.000	.000	1.159	1	.282	1.000	1.000	1.000
MyoInfarc	-5.49	2.595	4.482	1	.034	.004	.000	.665
OldMyoInfarc	-8.46	8.673	.953	1	.329	.000	.000	5070.198
PeriphVascDisDx	-.084	1.106	.006	1	.940	.920	.105	8.037
CerebroVascDis	1.276	1.414	.814	1	.367	3.583	.224	57.254
COPD	-.321	.337	.904	1	.342	.726	.375	1.405
Dementia	-.553	1.748	.100	1	.752	.575	.019	17.686
Paralysis	.181	4.648	.002	1	.969	1.199	.000	10841.24
Diabetes	1.386	.938	2.181	1	.140	3.998	.635	25.150
DiabetesSequelae	.848	1.182	.514	1	.473	2.334	.230	23.670
ChronicRenalFail	-2.51	1.347	3.482	1	.062	.081	.006	1.135
Rheum	-5.89	5.477	1.157	1	.282	.003	.000	126.996
a. Degree of freedom reduced because of constant or linearly dependent covariates								
b. Constant or Linearly Dependent Covariates S = Stratum effect. HistStageCombinary = .9635 + S ; Hormones = 0 + S ;								

Appendix C

Logistic and Conditional Cox Regression Output with Propensity Analysis

Quintile 1

Case Processing Summary			
Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	11518	100.0
	Missing Cases	0	.0
	Total	11518	100.0
Unselected Cases		0	.0
Total		11518	100.0

a. If weight is in effect, see classification table for the total number of cases.

b. The variable Hormones is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

Dependent Variable Encoding	
Original Value	Internal Value
0	0
1	1

Categorical Variables Codings							
			Parameter coding				
		Frequency	(1)	(2)	(3)	(4)	(5)
Marital Status	1	1220	.000	.000	.000	.000	.000
	2	7819	1.000	.000	.000	.000	.000
	3	70	.000	1.000	.000	.000	.000
	4	628	.000	.000	1.000	.000	.000
	5	756	.000	.000	.000	1.000	.000
	9	1025	.000	.000	.000	.000	1.000

Radiation 1	0	8099	.000	.000	.000	.000
	1	2190	1.000	.000	.000	.000
	2	420	.000	1.000	.000	.000
	4	513	.000	.000	1.000	.000
	9	296	.000	.000	.000	1.000
Age at Diagnosis	14	8684	.000	.000	.000	.000
Year 1	15	1337	1.000	.000	.000	.000
	16	729	.000	1.000	.000	.000
	17	473	.000	.000	1.000	.000
	18	295	.000	.000	.000	1.000
Grade 1	1	1107	.000			
	2	10411	1.000			
SEER Race Recode	1	8966	.000			
B	2	2552	1.000			

Block 0: Beginning Block

Classification Table[a,b]

			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 0	Mortality	0	11129	0	100.0
		1	389	0	.0
	Overall Percentage				96.6

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	Df	Sig.	Exp (B)
Step 0	Constant	-3.354	.052	4227.513	1	.000	.035

Variables not in the Equation[a]					
			Score	df	Sig.
Step 0		sPSA	4.919	1	.027
		Race	.022	1	.883
		Age	299.591	4	.000
		Age(1)	3.050	1	.081
		Age(2)	73.170	1	.000
		Age(3)	42.311	1	.000
		Age(4)	146.239	1	.000
		Grade	8.452	1	.004
		HistStageCombinary	162.673	1	.000
		MarStatus	47.226	5	.000
		MarStatus(1)	35.682	1	.000
		MarStatus(2)	.178	1	.673
		MarStatus(3)	.002	1	.962
		MarStatus(4)	13.236	1	.000
		MarStatus(5)	22.842	1	.000
		Radiation	15.807	4	.003
		Radiation(1)	11.713	1	.001
		Radiation(2)	1.326	1	.250
		Radiation(3)	4.334	1	.037
		Radiation(4)	.107	1	.744
		RadSurgCombinary	11.573	1	.001
		SurgCombinary	24.621	1	.000
		PctNonHSGrad	.002	1	.968
		PctHSonly	.027	1	.871
		PctSomeColl	1.820	1	.177
		Pct4yrColl	.231	1	.631
		MedIncome	.011	1	.916
		MyoInfarc	.872	1	.351
		OldMyoInfarc	1.607	1	.205
		CHF	12.176	1	.000
		PeriphVascDis	.980	1	.322
		CerebroVascDis	3.180	1	.075
		COPD	5.351	1	.021

		Dementia	48.764	1	.000
		Paralysis	2.503	1	.114
		Diabetes	1.570	1	.210
		DiabetesSequelae	.109	1	.741
		ChronicRenalFail	2.639	1	.104
		Rheum	3.126	1	.077
a. Residual Chi-Squares are not computed because of redundancies.					

Block 1: Method = Enter

Omnibus Tests of Model Coefficients				
		Chi-square	Df	Sig.
Step 1	Step	399.392	36	.000
	Block	399.392	36	.000
	Model	399.392	36	.000

Model Summary			
Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	3001.252[a]	.034	.133
a. Estimation terminated at iteration number 7 because parameter estimates changed by less than .001.			

Classification Table[a]				
			Predicted	
			Mortality	Percentage
	Observed		0	1	Correct
Step 1	Mortality	0	11127	2	100.0
		1	382	7	1.8
	Overall Percentage				96.7
a. The cut value is .500					

Variables in the Equation								
							95% C.I. for exp (B)	
	B	S.E.	Wald	df	Sig.	Exp (B)	Lower	Upper
sPSA	-.196	.108	3.321	1	.068	.822	.665	1.015
Race	.148	.159	.861	1	.353	1.159	.848	1.584
Age (66-69)			152.36	4	.000			
Age(1)(70-74)	.117	.181	.418	1	.518	1.124	.788	1.604
Age(2)(75-79)	.932	.180	26.755	1	.000	2.540	1.784	3.615
Age(3)(80-84)	1.211	.207	34.298	1	.000	3.356	2.238	5.033
Age(4)(85+)	2.201	.194	129.32	1	.000	9.034	6.182	13.201
Grade	-.063	.160	.155	1	.694	.939	.686	1.285
HistStageCombine	-1.655	.182	82.345	1	.000	.191	.134	.273
MarStatus			42.549	5	.000			
MarStatus(1)	-.563	.170	10.949	1	.001	.570	.408	.795
MarStatus(2)	.190	.626	.092	1	.762	1.209	.354	4.127
MarStatus(3)	-.164	.273	.362	1	.548	.849	.497	1.449
MarStatus(4)	-.233	.226	1.059	1	.304	.792	.509	1.234
MarStatus(5)	.493	.211	5.436	1	.020	1.637	1.082	2.477
Radiation			19.740	4	.001			
Radiation(1)	.524	.146	12.845	1	.000	1.688	1.268	2.248
Radiation(2)	.178	.341	.274	1	.601	1.195	.613	2.331
Radiation(3)	-.013	.355	.001	1	.970	.987	.492	1.979
Radiation(4)	-.804	.352	5.208	1	.022	.448	.224	.893
RadSurgCombine	.090	.237	.143	1	.706	1.094	.687	1.741
SurgCombinary	1.112	.155	51.436	1	.000	3.039	2.243	4.118
PctNonHSGrad	-.014	.040	.121	1	.728	.986	.911	1.067
PctHSonly	-.002	.041	.002	1	.964	.998	.922	1.081
PctSomeColl	-.025	.041	.380	1	.538	.975	.900	1.056
Pct4yrColl	-.009	.041	.044	1	.834	.992	.916	1.074
MedIncome	.000	.000	.000	1	.990	1.000	1.000	1.000
MyoInfarc	-.480	1.59	.090	1	.764	.619	.027	14.224
OldMyoInfarc	4.759	5.35	.789	1	.374	116.632	.003	4239913.2
CHF	.370	.230	2.593	1	.107	1.448	.923	2.271
PeriphVascDis	-.392	.801	.240	1	.624	.676	.141	3.245
CerebroVascDis	-.203	.815	.062	1	.803	.816	.165	4.030

COPD	.231	.210	1.212	1	.271	1.260	.835	1.900
Dementia	2.521	.486	26.958	1	.000	12.440	4.803	32.220
Paralysis	2.334	1.30	3.186	1	.074	10.324	.795	134.006
Diabetes	.604	.739	.668	1	.414	1.830	.430	7.792
DiabetesSequelae	-1.027	.950	1.169	1	.280	.358	.056	2.305
ChronicRenalFail	.809	.498	2.639	1	.104	2.246	.846	5.963
Rheum	3.552	4.69	.574	1	.449	34.896	.004	343248.32
Constant	-1.596	4.04	.156	1	.693	.203		

a. Variable(s) entered on step 1: sPSA, Race, Age, Grade, HistStageCombinary, MarStatus, Radiation, RadSurgCombinary, SurgCombinary, PctNonHSGrad, PctHSonly, PctSomeColl, Pct4yrColl, MedIncome, MyoInfarc, OldMyoInfarc, CHF, PeriphVascDisDx, CerebroVascDis, COPD, Dementia, Paralysis, Diabetes, DiabetesSequelae, ChronicRenalFail, Rheum.

Conditional Cox Regression Quintile 1

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	389	3.4%
	Censored	209	1.8%
	Total	598	5.2%
Cases dropped	Cases with missing values	0	.0%
	Cases with negative time	0	.0%
	Censored cases before the earliest event in a stratum	10920	94.8%
	Total	10920	94.8%
Total		11518	100.0%

a. Dependent Variable: Survival time recode (total # of months)

Categorical Variable Codings[b,c,d,e,f]

		Frequency	(1)	(2)	(3)	(4)	(5)
Age[a]	14	8684	0	0	0	0	
	15	1337	1	0	0	0	
	16	729	0	1	0	0	
	17	473	0	0	1	0	
	18	295	0	0	0	1	
Grade[a]	1	1107	0				
	2	10411	1				
MarStatus[a]	1	1220	0	0	0	0	0
	2	7819	1	0	0	0	0
	3	70	0	1	0	0	0
	4	628	0	0	1	0	0
	5	756	0	0	0	1	0
	9	1025	0	0	0	0	1
Race[a]	1	8966	0				
	2	2552	1				
Radiation[a]	0	8099	0	0	0	0	
	1	2190	1	0	0	0	
	2	420	0	1	0	0	
	4	513	0	0	1	0	
	9	296	0	0	0	1	

a. Indicator Parameter Coding
b. Category variable: Age (Age at Diagnosis Year 1)
c. Category variable: Grade (Grade 1)
d. Category variable: MarStatus (Marital Status)
e. Category variable: Race (SEER Race Recode B)
f. Category variable: Radiation (Radiation 1)

Block 0: Beginning Block

Omnibus Tests of Model Coefficients
-2 Log Likelihood
300.826

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]									
-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
	Chi-square	Df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
205.389	73.469	34	.000	95.437	34	.000	95.437	34	.000
a. Beginning Block Number 1. Method = Enter									

Variables in the Equation								
							95.0% CI for Exp (B)	
	B	SE	Wald	Df	Sig.	Exp (B)	Lower	Upper
sPSA	.019	.185	.010	1	.919	1.019	.710	1.463
Race	2.918	4.258	.470	1	.493	18.506	.004	77918.81
Age			16.470	4	.002			
Age(1)	-4.051	5.699	.505	1	.477	.017	.000	1234.359
Age(2)	-3.213	5.897	.297	1	.586	.040	.000	4205.373
Age(3)	-1.334	4.824	.076	1	.782	.263	.000	3366.156
Age(4)	-.011	3.060	.000	1	.997	.989	.002	397.657
Grade	-.826	1.429	.334	1	.563	.438	.027	7.203
HistStageCombine			.	0[a]	.			
MarStatus			6.370	5	.272			
MarStatus(1)	-1.785	2.083	.735	1	.391	.168	.003	9.949
MarStatus(2)	13.848	120.3	.013	1	.908	1033086.	.000	2.975E108
MarStatus(3)	-.478	.995	.230	1	.631	.620	.088	4.364
MarStatus(4)	.843	1.583	.283	1	.595	2.322	.104	51.689
MarStatus(5)	-.487	1.216	.161	1	.689	.614	.057	6.657
Radiation			3.317	4	.506			
Radiation(1)	.212	.442	.230	1	.631	1.236	.520	2.939
Radiation(2)	-1.960	2.318	.716	1	.398	.141	.001	13.223
Radiation(3)	-1.196	.907	1.737	1	.188	.302	.051	1.791
Radiation(4)	.632	1.049	.363	1	.547	1.882	.241	14.712
RadSurgCombinary	1.070	.745	2.064	1	.151	2.916	.677	12.557
SurgCombinary	1.259	3.783	.111	1	.739	3.522	.002	5850.057
Hormones			.	0[a]	.			

PctNonHSGrad	-.060	.233	.065	1	.798	.942	.596	1.488
PctHSonly	-.051	.238	.045	1	.831	.951	.596	1.515
PctSomeColl	-.180	.247	.528	1	.468	.835	.514	1.357
Pct4yrColl	-.103	.245	.178	1	.673	.902	.558	1.457
MedIncome	.000	.000	.100	1	.752	1.000	1.000	1.000
MyoInfarc	-9.569	4.094	5.462	1	.019	.000	.000	.213
OldMyoInfarc	55.089	51.74	1.133	1	.287	8.407E23	.000	9.381E67
CHF	3.442	5.198	.439	1	.508	31.263	.001	830301.47
PeriphVascDis	.233	3.832	.004	1	.952	1.262	.001	2308.350
CerebroVascDis	8.999	8.123	1.228	1	.268	8097.961	.001	6.643E10
COPD	2.301	3.144	.536	1	.464	9.982	.021	4731.409
Dementia	7.801	10.68	.533	1	.465	2443.634	.000	3.040E12
Paralysis	27.262	169.6	.026	1	.872	6.912E11	.000	1.656E156
Diabetes	5.395	2.884	3.500	1	.061	220.360	.773	62793.265
DiabetesSequelae	-.960	3.458	.077	1	.781	.383	.000	335.926
ChronicRenalFail	7.090	11.64	.371	1	.543	1199.333	.000	9.729E12
Rheum			.	0[a]	.			
a. Degree of freedom reduced because of constant or linearly dependent covariates								

Appendix D

Logistic and Conditional Cox Regression Output with Propensity Analysis

Quintile 2

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	8084	100.0
	Missing Cases	0	.0
	Total	8084	100.0
Unselected Cases		0	.0
Total		8084	100.0

a. If weight is in effect, see classification table for the total number of cases.

b. The variable HistStageCombinary is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

c. The variable Hormones is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

Dependent Variable Encoding

Original Value	Internal Value
0	0
1	1

Categorical Variables Codings

			Parameter coding				
		Frequency	(1)	(2)	(3)	(4)	(5)
Marital Status	1	559	.000	.000	.000	.000	.000
	2	5614	1.000	.000	.000	.000	.000

	3	29	.000	1.000	.000	.000	.000
	4	375	.000	.000	1.000	.000	.000
	5	656	.000	.000	.000	1.000	.000
	9	851	.000	.000	.000	.000	1.000
Radiation 1	0	4463	.000	.000	.000	.000	
	1	2233	1.000	.000	.000	.000	
	2	638	.000	1.000	.000	.000	
	4	619	.000	.000	1.000	.000	
	9	131	.000	.000	.000	1.000	
Age at Diagnosis Year	14	3709	.000	.000	.000	.000	
1	15	2323	1.000	.000	.000	.000	
	16	1213	.000	1.000	.000	.000	
	17	591	.000	.000	1.000	.000	
	18	248	.000	.000	.000	1.000	
Grade 1	1	747	.000				
	2	7337	1.000				
SEER Race Recode B	1	7040	.000				
	2	1044	1.000				

Block 0: Beginning Block

Classification Table[a,b]

			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 0	Mortality	0	7825	0	100.0
		1	259	0	.0
	Overall Percentage				96.8

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	Df	Sig.	Exp (B)
Step 0	Constant	-3.408	.063	2912.198	1	.000	.033

Variables not in the Equation[a]

			Score	Df	Sig.
Step 0	Variables	sPSA	.483	1	.487
		Race	1.475	1	.225
		Age	103.348	4	.000
		Age(1)	.229	1	.633
		Age(2)	16.743	1	.000
		Age(3)	46.365	1	.000
		Age(4)	16.392	1	.000
		Grade	5.825	1	.016
		MarStatus	11.304	5	.046
		MarStatus(1)	8.987	1	.003
		MarStatus(2)	.006	1	.940
		MarStatus(3)	.093	1	.761
		MarStatus(4)	3.409	1	.065
		MarStatus(5)	4.880	1	.027
		Radiation	21.045	4	.000
		Radiation(1)	2.217	1	.136
		Radiation(2)	4.890	1	.027
		Radiation(3)	3.460	1	.063
		Radiation(4)	4.407	1	.036
		RadSurgCombine	.004	1	.951
		SurgCombinary	68.383	1	.000
		PctNonHSGrad	2.160	1	.142
		PctHSonly	.871	1	.351
		PctSomeColl	.338	1	.561
		Pct4yrColl	.438	1	.508
		MedIncome	.012	1	.912
		MyoInfarc	.339	1	.560
		OldMyoInfarc	.021	1	.885
		CHF	.080	1	.778
		PeriphVascDis	.883	1	.347
		CerebroVascDis	2.288	1	.130
		COPD	.924	1	.336
		Dementia	.033	1	.856
		Paralysis	.398	1	.528

	Diabetes	.000	1	.999
	DiabetesSequelae	.222	1	.638
	ChronicRenalFail	.531	1	.466
	Rheum	.516	1	.472
a. Residual Chi-Squares are not computed because of redundancies.				

Block 1: Method = Enter

Omnibus Tests of Model Coefficients				
		Chi-square	Df	Sig.
Step 1	Step	153.657	35	.000
	Block	153.657	35	.000
	Model	153.657	35	.000

Model Summary			
Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	2138.297[a]	.019	.076
a. Estimation terminated at iteration number 20 because maximum iterations have been reached. Final solution cannot be found.			

Classification Table[a]					
			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 1	Mortality	0	7825	0	100.0
		1	259	0	.0
	Overall Percentage				96.8
a. The cut value is .500					

Variables in the Equation								
							95% C.I. for EXP (B)	
	B	S.E.	Wald	df	Sig.	Exp (B)	Lower	Upper
sPSA	-.101	.128	.618	1	.432	.904	.703	1.163
Race	.339	.520	.424	1	.515	1.403	.506	3.892
Age			44.95	4	.000			
Age(1)	-.349	.635	.303	1	.582	.705	.203	2.447
Age(2)	.281	.663	.180	1	.672	1.324	.361	4.857
Age(3)	.790	.574	1.895	1	.169	2.204	.715	6.790
Age(4)	1.004	.444	5.099	1	.024	2.728	1.142	6.520
Grade	-.104	.234	.197	1	.657	.901	.570	1.426
MarStatus			8.427	5	.134			
MarStatus(1)	-.392	.307	1.632	1	.201	.676	.370	1.233
MarStatus(2)	.053	1.051	.003	1	.960	1.055	.135	8.266
MarStatus(3)	-.121	.387	.098	1	.754	.886	.415	1.893
MarStatus(4)	-.211	.321	.430	1	.512	.810	.431	1.520
MarStatus(5)	.232	.295	.616	1	.433	1.261	.707	2.248
Radiation			.749	4	.945			
Radiation(1)	.002	.169	.000	1	.989	1.002	.720	1.396
Radiation(2)	-.339	.405	.699	1	.403	.713	.322	1.577
Radiation(3)	-.030	.320	.009	1	.926	.971	.518	1.818
Radiation(4)	-18.528	3431.1	.000	1	.996	.000	.000	.
RadSurgCombine	-.290	.393	.544	1	.461	.748	.347	1.617
SurgCombinary	1.135	.460	6.088	1	.014	3.110	1.263	7.661
PctNonHSGrad	-.172	.111	2.417	1	.120	.842	.677	1.046
PctHSonly	-.145	.111	1.696	1	.193	.865	.696	1.076
PctSomeColl	-.172	.112	2.374	1	.123	.842	.677	1.048
Pct4yrColl	-.155	.112	1.939	1	.164	.856	.688	1.065
MedIncome	.000	.000	.255	1	.613	1.000	1.000	1.000
MyoInfarc	1.143	2.255	.257	1	.612	3.136	.038	260.517
OldMyoInfarc	-3.293	10.988	.090	1	.764	.037	.000	8.369E7
CHF	.618	.733	.709	1	.400	1.855	.441	7.808

PeriphVascDis	.774	1.106	.490	1	.484	2.169	.248	18.959
CerebroVascDis	1.507	1.345	1.256	1	.262	4.513	.324	62.965
COPD	.119	.409	.084	1	.772	1.126	.505	2.511
Dementia	-21.279	51728.	.000	1	1.00	.000	.000	.
Paralysis	-44.863	28956.	.000	1	.999	.000	.000	.
Diabetes	-.026	1.002	.001	1	.979	.974	.137	6.946
DiabetesSequelae	-.742	1.412	.276	1	.599	.476	.030	7.580
ChronicRenalFail	-24.968	14582	.000	1	.999	.000	.000	.
Rheum	1.789	5.908	.092	1	.762	5.984	.000	639306
Constant	12.259	11.097	1.220	1	.269	210850.6		

a. Variable(s) entered on step 1: sPSA, Race, Age, Grade, MarStatus, Radiation, RadSurgCombinary, SurgCombinary, PctNonHSGrad, PctHSonly, PctSomeColl, Pct4yrColl, MedIncome, MyoInfarc, OldMyoInfarc, CHF, PeriphVascDisDx, CerebroVascDis, COPD, Dementia, Paralysis, Diabetes, DiabetesSequelae, ChronicRenalFail, Rheum.

Conditional Cox Regression for Quintile 2

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	259	3.2%
	Censored	125	1.5%
	Total	384	4.8%
Cases dropped	Cases with missing values	0	.0%
	Cases with negative time	0	.0%
	Censored cases before the earliest event in a stratum	7700	95.2%
	Total	7700	95.2%
Total		8084	100.0%

a. Dependent Variable: Survival time recode (total # of months)

Categorical Variable Codings[b,c,d,e,f]

		Frequency	(1)	(2)	(3)	(4)	(5)
Age[a]	14	3709	0	0	0	0	
	15	2323	1	0	0	0	
	16	1213	0	1	0	0	
	17	591	0	0	1	0	
	18	248	0	0	0	1	
Grade[a]	1	747	1				
	2	7337	0				
MarStatus[a]	1	559	0	0	0	0	0
	2	5614	1	0	0	0	0
	3	29	0	1	0	0	0
	4	375	0	0	1	0	0
	5	656	0	0	0	1	0
	9	851	0	0	0	0	1
Race[a]	1	7040	0				
	2	1044	1				
Radiation[a]	0	4463	0	0	0	0	
	1	2233	1	0	0	0	
	2	638	0	1	0	0	
	4	619	0	0	1	0	
	9	131	0	0	0	1	

a. Indicator Parameter Coding
b. Category variable: Age (Age at Diagnosis Year 1)
c. Category variable: Grade (Grade 1)
d. Category variable: MarStatus (Marital Status)
e. Category variable: Race (SEER Race Recode B)
f. Category variable: Radiation (Radiation 1)

Block 0: Beginning Block

Omnibus Tests of Model Coefficients
-2 Log Likelihood

Omnibus Tests of Model Coefficients
-2 Log Likelihood
176.059

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]									
-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
	Chi-square	Df	Sig.	Chi-square	Df	Sig.	Chi-square	df	Sig.
87.830	62.430	31	.001	88.229	31	.000	88.229	31	.000
a. Beginning Block Number 1. Method = Enter									

Variables in the Equation								
							95.0% CI for Exp (B)	
	B	SE	Wald	Df	Sig.	Exp (B)	Lower	Upper
sPSA	-.292	.316	.856	1	.355	.747	.402	1.387
Race	-1.215	39.584	.001	1	.976	.297	.000	1.468E33
Age			12.255	4	.016			
Age(1)	-2.272	40.099	.003	1	.955	.103	.000	1.400E33
Age(2)	-1.202	40.183	.001	1	.976	.301	.000	4.809E33
Age(3)	2.297	39.807	.003	1	.954	9.940	.000	7.612E34
Age(4)	12.24	54.696	.050	1	.823	208864.64	.000	7.534E51
Grade	-4.511	2.527	3.186	1	.074	.011	.000	1.556
HistStageCombine			.	0[a]	.			
MarStatus			5.068	5	.408			
MarStatus(1)	-5.148	3.667	1.971	1	.160	.006	.000	7.689
MarStatus(2)	18.73	168.61	.012	1	.912	1.367E8	.000	4.601E151
MarStatus(3)	-.864	1.934	.200	1	.655	.421	.010	18.647
MarStatus(4)	-2.848	2.581	1.217	1	.270	.058	.000	9.128
MarStatus(5)	-1.838	2.174	.715	1	.398	.159	.002	11.270

Radiation			8.612	4	.072			
Radiation(1)	-2.406	.839	8.235	1	.004	.090	.017	.466
Radiation(2)	-6.113	4.064	2.262	1	.133	.002	.000	6.378
Radiation(3)	-1.234	1.173	1.106	1	.293	.291	.029	2.903
Radiation(4)	-19.1	71.335	.072	1	.789	.000	.000	2.653E52
RadSurgCombine	2.972	1.580	3.539	1	.060	19.523	.883	431.553
SurgCombinary	-4.439	39.456	.013	1	.910	.012	.000	4.546E31
Hormones			.	0[a]	.			
PctNonHSGrad	.179	.390	.211	1	.646	1.196	.557	2.568
PctHSonly	.291	.384	.574	1	.449	1.338	.630	2.841
PctSomeColl	.060	.440	.018	1	.892	1.062	.448	2.513
Pct4yrColl	.000	.438	.000	1	1.000	1.000	.424	2.358
MedIncome	.000	.000	2.083	1	.149	1.000	1.000	1.000
MyoInfarc	6.937	444.07	.000	1	.988	1029.705	.000	.
OldMyoInfarc	-15.04	665.60	.001	1	.982	.000	.000	.
CHF	-2.405	45.483	.003	1	.958	.090	.000	4.685E37
PeriphVascDis	-8.258	93.888	.008	1	.930	.000	.000	2.145E76
CerebroVascDis	58.74	205.53	.082	1	.775	3.270E25	.000	2.900E200
COPD	6.793	4.973	1.866	1	.172	891.397	.052	1.524E7
Dementia			.	0[a]	.			
Paralysis			.	0[a]	.			
Diabetes	-.192	4.230	.002	1	.964	.825	.000	3290.749
DiabetesSequelae	4.883	3.741	1.703	1	.192	132.022	.086	201994.02
ChronicRenalFail			.	0[a]	.			
Rheum			.	0[a]	.			

a. Degree of freedom reduced because of constant or linearly dependent covariates

Appendix E

Logistic and Conditional Cox Regression Output with Propensity Analysis

Quintile 3

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	11496	100.0
	Missing Cases	0	.0
	Total	11496	100.0
Unselected Cases		0	.0
Total		11496	100.0

a. If weight is in effect, see classification table for the total number of cases.

b. The variable HistStageCombinary is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

c. The variable Hormones is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

d. The variable DEMENTIA (1) is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

Dependent Variable Encoding

Original Value	Internal Value
0	0
1	1

Categorical Variables Codings

			Parameter coding				
		Frequency	(1)	(2)	(3)	(4)	(5)
Marital Status	1	612	.000	.000	.000	.000	.000
	2	8649	1.000	.000	.000	.000	.000
	3	29	.000	1.000	.000	.000	.000
	4	350	.000	.000	1.000	.000	.000
	5	846	.000	.000	.000	1.000	.000
	9	1010	.000	.000	.000	.000	1.000
Radiation 1	0	6453	.000	.000	.000	.000	
	1	2664	1.000	.000	.000	.000	
	2	1566	.000	1.000	.000	.000	
	4	695	.000	.000	1.000	.000	
	9	118	.000	.000	.000	1.000	
Age at Diagnosis Year	14	2609	.000	.000	.000	.000	
1	15	4731	1.000	.000	.000	.000	
	16	2469	.000	1.000	.000	.000	
	17	1130	.000	.000	1.000	.000	
	18	557	.000	.000	.000	1.000	
Grade 1	1	699	.000				
	2	10797	1.000				
SEER Race Recode B	1	10784	.000				
	2	712	1.000				

Block 0: Beginning Block

Classification Table[a,b]

			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 0	Mortality	0	11085	0	100.0
		1	411	0	.0
	Overall Percentage				96.4

a. Constant is included in the model.

Classification Table[a,b]					
			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 0	Mortality	0	11085	0	100.0
		1	411	0	.0
	Overall Percentage				96.4
a. Constant is included in the model.					
b. The cut value is .500					

Variables in the Equation							
		B	S.E.	Wald	Df	Sig.	Exp (B)
Step 0	Constant	-3.295	.050	4302.065	1	.000	.037

Variables not in the Equation[a]				
		Score	Df	Sig.
Variables	sPSA	6.563	1	.010
	Race	.862	1	.353
	Age	88.958	4	.000
	Age(1)	5.579	1	.018
	Age(2)	48.152	1	.000
	Age(3)	12.082	1	.001
	Age(4)	.521	1	.470
	Grade	2.171	1	.141
	MarStatus	35.462	5	.000
	MarStatus(1)	19.778	1	.000
	MarStatus(2)	1.078	1	.299
	MarStatus(3)	.020	1	.887
	MarStatus(4)	2.225	1	.136
	MarStatus(5)	30.046	1	.000
	Radiation	38.330	4	.000
	Radiation(1)	3.980	1	.046
	Radiation(2)	27.772	1	.000

	Radiation(3)	4.308	1	.038
	Radiation(4)	2.573	1	.109
	RadSurgCombinary	1.845	1	.174
	SurgCombinary	40.731	1	.000
	PctNonHSGrad	.343	1	.558
	PctHSonly	.415	1	.519
	PctSomeColl	1.233	1	.267
	Pct4yrColl	.090	1	.764
	MedIncome	.416	1	.519
	MyoInfarc	.796	1	.372
	OldMyoInfarc	.226	1	.634
	CHF	1.926	1	.165
	PeriphVascDisDx	.280	1	.597
	CerebroVascDis	.708	1	.400
	COPD	.854	1	.355
	Paralysis	.111	1	.739
	Diabetes	1.754	1	.185
	DiabetesSequelae	2.324	1	.127
	ChronicRenalFail	.037	1	.847
	Rheum	.594	1	.441
a. Residual Chi-Squares are not computed because of redundancies.				

Block 1: Method = Enter

Omnibus Tests of Model Coefficients				
		Chi-square	Df	Sig.
Step 1	Step	178.886	34	.000
	Block	178.886	34	.000
	Model	178.886	34	.000

Model Summary			
Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	3366.457[a]	.015	.058

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	3366.457[a]	.015	.058

a. Estimation terminated at iteration number 20 because maximum iterations have been reached. Final solution cannot be found.

Classification Table[a]

			Predicted Mortality		Percentage Correct
	Observed		0	1	
Step 1	Mortality	0	11085	0	100.0
		1	411	0	.0
	Overall Percentage				96.4

a. The cut value is .500

Variables in the Equation

	B	S.E.	Wald	Df	Sig.	Exp (B)	95% C.I. for Exp (B)	
							Lower	Upper
sPSA	-.297	.102	8.407	1	.004	.743	.608	.908
Race	.551	.375	2.155	1	.142	1.735	.831	3.619
Age			39.48	4	.000			
Age(1)	-.493	.437	1.276	1	.259	.611	.259	1.437
Age(2)	.163	.455	.128	1	.720	1.177	.483	2.870
Age(3)	.324	.400	.655	1	.418	1.383	.631	3.031
Age(4)	.388	.356	1.189	1	.275	1.474	.734	2.959
Grade	-.312	.214	2.121	1	.145	.732	.481	1.114
MarStatus			29.91	5	.000			
MarStatus(1)	-.428	.273	2.452	1	.117	.652	.381	1.114
MarStatus(2)	-17.99	7372.3	.000	1	.998	.000	.000	.
MarStatus(3)	.005	.365	.000	1	.990	1.005	.491	2.056
MarStatus(4)	-.073	.293	.061	1	.804	.930	.524	1.651
MarStatus(5)	.481	.265	3.276	1	.070	1.617	.961	2.721

Radiation			13.92	4	.008			
Radiation(1)	.114	.128	.802	1	.371	1.121	.873	1.439
Radiation(2)	-.766	.302	6.452	1	.011	.465	.257	.839
Radiation(3)	-.300	.283	1.127	1	.288	.741	.425	1.289
Radiation(4)	-2.011	1.013	3.939	1	.047	.134	.018	.975
RadSurgCombine	.131	.268	.238	1	.625	1.140	.674	1.927
SurgCombinary	1.089	.296	13.50	1	.000	2.972	1.662	5.313
PctNonHSGrad	-.023	.025	.813	1	.367	.978	.930	1.027
PctHSonly	-.015	.025	.336	1	.562	.985	.937	1.036
PctSomeColl	-.039	.026	2.237	1	.135	.961	.913	1.012
Pct4yrColl	-.026	.026	1.012	1	.314	.974	.926	1.025
MedIncome	.000	.000	.000	1	.999	1.000	1.000	1.000
MyoInfarc	-1.797	2.481	.525	1	.469	.166	.001	21.425
OldMyoInfarc	4.317	9.259	.217	1	.641	74.926	.000	5.703E9
CHF	-.285	.895	.101	1	.751	.752	.130	4.349
PeriphVascDis	-.137	1.207	.013	1	.909	.872	.082	9.277
CerebroVascDis	-.055	1.246	.002	1	.965	.946	.082	10.878
COPD	.157	.358	.193	1	.660	1.170	.580	2.360
Paralysis	-42.24	58618.	.000	1	.999	.000	.000	.
Diabetes	.922	.836	1.214	1	.270	2.513	.488	12.942
DiabetesSequelae	.944	.907	1.083	1	.298	2.571	.434	15.222
ChronicRenalFail	-23.03	59281.	.000	1	1.000	.000	.000	.
Rheum	4.447	5.217	.727	1	.394	85.366	.003	2353126
Constant	-.661	2.546	.067	1	.795	.516		

a. Variable(s) entered on step 1: sPSA, Race, Age, Grade, MarStatus, Radiation, RadSurgCombinary, SurgCombinary, PctNonHSGrad, PctHSonly, PctSomeColl, Pct4yrColl, MedIncome, MyoInfarc, OldMyoInfarc, CHF, PeriphVascDisDx, CerebroVascDis, COPD, Paralysis, Diabetes, DiabetesSequelae, ChronicRenalFail, Rheum.

Conditional Cox Regression for Quintile 3

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	411	3.6%
	Censored	208	1.8%
	Total	619	5.4%
Cases dropped	Cases with missing values	0	.0%
	Cases with negative time	0	.0%
	Censored cases before the earliest event in a stratum	10877	94.6%
	Total	10877	94.6%
Total		11496	100.0%

a. Dependent Variable: Survival time recode (total # of months)

Categorical Variable Codings[b,c,d,e,f]

		Frequency	(1)	(2)	(3)	(4)	(5)
Age[a]	14	2609	1	0	0	0	
	15	4731	0	1	0	0	
	16	2469	0	0	1	0	
	17	1130	0	0	0	1	
	18	557	0	0	0	0	
Grade[a]	1	699	0				
	2	10797	1				
MarStatus[a]	1	612	0	0	0	0	0
	2	8649	1	0	0	0	0
	3	29	0	1	0	0	0
	4	350	0	0	1	0	0
	5	846	0	0	0	1	0
	9	1010	0	0	0	0	1
Race[a]	1	10784	0				
	2	712	1				

Radiation[a]	0	6453	0	0	0	0
	1	2664	1	0	0	0
	2	1566	0	1	0	0
	4	695	0	0	1	0
	9	118	0	0	0	1

a. Indicator Parameter Coding
b. Category variable: Age (Age at Diagnosis Year 1)
c. Category variable: Grade (Grade 1)
d. Category variable: MarStatus (Marital Status)
e. Category variable: Race (SEER Race Recode B)
f. Category variable: Radiation (Radiation 1)

Block 0: Beginning Block

Omnibus Tests of Model Coefficients
-2 Log Likelihood
295.281

Omnibus Tests of Model Coefficients[a]

-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
	Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
229.252	56.658	30	.002	66.029	30	.000	66.029	30	.000

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

	B	SE	Wald	Df	Sig.	Exp (B)	95.0% CI for Exp (B)	
							Lower	Upper
sPSA	-.199	.171	1.365	1	.243	.819	.586	1.145
Race	1.098	1.255	.765	1	.382	2.997	.256	35.055
Age			6.083	4	.193			
Age(1)	-.943	1.582	.356	1	.551	.389	.018	8.645
Age(2)	-.454	1.651	.076	1	.783	.635	.025	16.152

Age(3)	-.301	1.458	.043	1	.836	.740	.042	12.886
Age(4)	.574	1.178	.238	1	.626	1.776	.177	17.868
Grade	-.312	.609	.263	1	.608	.732	.222	2.412
HistStageCombine			.	0[a]	.			
MarStatus			4.565	4[a]	.335			
MarStatus(1)	.131	.768	.029	1	.865	1.140	.253	5.133
MarStatus(3)	.481	.907	.281	1	.596	1.618	.273	9.579
MarStatus(4)	.091	.747	.015	1	.903	1.095	.253	4.736
MarStatus(5)	.996	.701	2.021	1	.155	2.708	.686	10.696
Radiation			7.547	4	.110			
Radiation(1)	-.705	.330	4.570	1	.033	.494	.259	.943
Radiation(2)	-1.32	.840	2.482	1	.115	.266	.051	1.381
Radiation(3)	-1.28	.572	5.018	1	.025	.277	.090	.852
Radiation(4)	.269	1.592	.029	1	.866	1.309	.058	29.640
RadSurgCombined	2.359	.734	10.331	1	.001	10.576	2.510	44.558
SurgCombinary	-.048	1.088	.002	1	.964	.953	.113	8.034
Hormones			.	0[a]	.			
PctNonHSGrad	-.469	.225	4.329	1	.037	.626	.402	.973
PctHSonly	-.450	.223	4.080	1	.043	.637	.412	.987
PctSomeColl	-.504	.226	4.958	1	.026	.604	.388	.941
Pct4yrColl	-.497	.226	4.843	1	.028	.608	.391	.947
MedIncome	.000	.000	1.824	1	.177	1.000	1.000	1.000
MyoInfarc	-40.9	510.315	.006	1	.936	.000	.000	.
OldMyoInfarc	-21.	19.650	1.153	1	.283	.000	.000	3.642E7
PeriphVascDisDx	-2.42	3.043	.632	1	.427	.089	.000	34.640
CerebroVascDis	.146	3.701	.002	1	.968	1.158	.001	1637.211
COPD	-.435	1.046	.173	1	.677	.647	.083	5.022
Dementia			.	0[a]	.			
Paralysis			.	0[a]	.			
Diabetes	-.691	2.001	.119	1	.730	.501	.010	25.315
DiabetesSequelae	2.520	2.735	.849	1	.357	12.424	.058	2642.014
ChronicRenalFail			.	0[a]	.			
Rheum	-6.96	11.814	.348	1	.555	.001	.000	1.070E7
a. Degree of freedom reduced because of constant or linearly dependent covariates								

Appendix F

Logistic and Conditional Cox Regression Output with Propensity Analysis

Quintile 4

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	7900	100.0
	Missing Cases	0	.0
	Total	7900	100.0
Unselected Cases		0	.0
Total		7900	100.0

a. If weight is in effect, see classification table for the total number of cases.

b. The variable HistStageCombinary is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

c. The variable Hormones is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

d. The variable DEMENTIA (1) is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

e. The variable CHRONIC RENAL FAILURE (2) is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

Categorical Variables Codings

			Parameter coding				
		Frequency	(1)	(2)	(3)	(4)	(5)
Marital Status	1	474	.000	.000	.000	.000	.000
	2	5316	1.000	.000	.000	.000	.000
	3	25	.000	1.000	.000	.000	.000
	4	260	.000	.000	1.000	.000	.000
	5	764	.000	.000	.000	1.000	.000
	9	1061	.000	.000	.000	.000	1.000
Radiation	0	3960	.000	.000	.000	.000	
	1	2467	1.000	.000	.000	.000	
	2	827	.000	1.000	.000	.000	
	4	595	.000	.000	1.000	.000	
	9	51	.000	.000	.000	1.000	
Age at Diagnosis	14	372	.000	.000	.000	.000	
	15	3491	1.000	.000	.000	.000	
Year 1	16	2452	.000	1.000	.000	.000	
	17	1331	.000	.000	1.000	.000	
	18	254	.000	.000	.000	1.000	
Grade 1	1	431	.000				
	2	7469	1.000				
SEER	1	7819	.000				
Race Recode B	2	81	1.000				

Block 0: Beginning Block

Classification Table[a,b]

			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 0	Mortality	0	7666	0	100.0
		1	234	0	.0
	Overall Percentage				97.0

a. Constant is included in the model.

Classification Table[a,b]

			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 0	Mortality	0	7666	0	100.0
		1	234	0	.0
	Overall Percentage				97.0

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp (B)
Step 0	Constant	-3.489	.066	2764.500	1	.000	.031

Variables not in the Equation[a]

		Score	df	Sig.
Step 0	sPSA	.282	1	.595
	Race	.850	1	.357
	Age	34.616	4	.000
	Age(1)	11.524	1	.001
	Age(2)	.234	1	.629
	Age(3)	14.633	1	.000
	Age(4)	10.169	1	.001
	Grade	.266	1	.606
	MarStatus	13.682	5	.018
	MarStatus(1)	1.791	1	.181
	MarStatus(2)	2.215	1	.137
	MarStatus(3)	1.010	1	.315
	MarStatus(4)	.664	1	.415
	MarStatus(5)	10.404	1	.001
	Radiation	20.819	4	.000
	Radiation(1)	4.659	1	.031
	Radiation(2)	7.337	1	.007
	Radiation(3)	1.352	1	.245
	Radiation(4)	1.523	1	.217
	RadSurgCombinary	.304	1	.582
	SurgCombinary	1.479	1	.224

PctNonHSGrad	4.118	1	.042
PctHSonly	8.222	1	.004
PctSomeColl	1.892	1	.169
Pct4yrColl	5.891	1	.015
MedIncome	3.544	1	.060
MyoInfarc	.124	1	.724
OldMyoInfarc	.006	1	.936
CHF	.551	1	.458
PeriphVascDis	2.537	1	.111
CerebroVascDis	.030	1	.862
COPD	1.650	1	.199
Paralysis	.031	1	.861
Diabetes	.082	1	.775
DiabetesSequelae	12.352	1	.000
Rheum	.100	1	.752

a. Residual Chi-Squares are not computed because of redundancies.

Block 1: Method = Enter

Omnibus Tests of Model Coefficients

		Chi-square	Df	Sig.
Step 1	Step	72.722	33	.000
	Block	72.722	33	.000
	Model	72.722	33	.000

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	2035.308[a]	.009	.039

a. Estimation terminated at iteration number 20 because maximum iterations have been reached. Final solution cannot be found.

Classification Table[a]

			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 1	Mortality	0	7666	0	100.0
		1	234	0	.0
	Overall Percentage				97.0

a. The cut value is .500

Variables in the Equation

							95% C.I. for Exp (B)	
	B	S.E.	Wald	df	Sig.	Exp (B)	Lower	Upper
sPSA	.075	.142	.277	1	.599	1.077	.816	1.422
Race	-.608	1.194	.259	1	.611	.545	.052	5.652
Age			18.35	4	.001			
Age(1)	.968	1.033	.878	1	.349	2.631	.348	19.917
Age(2)	1.272	1.068	1.41	1	.234	3.569	.440	28.954
Age(3)	1.628	.958	2.88	1	.089	5.093	.779	33.285
Age(4)	1.816	.827	4.81	1	.028	6.150	1.215	31.135
Grade	.174	.377	.214	1	.644	1.190	.569	2.490
MarStatus			8.23	5	.144			
MarStatus(1)	.067	.419	.025	1	.873	1.069	.470	2.430
MarStatus(2)	1.109	.813	1.86	1	.173	3.030	.616	14.909
MarStatus(3)	-.210	.551	.145	1	.703	.811	.276	2.385
MarStatus(4)	-.119	.419	.081	1	.777	.888	.391	2.019
MarStatus(5)	.464	.364	1.62	1	.202	1.590	.780	3.242
Radiation			3.387	4	.495			
Radiation(1)	-.243	.170	2.05	1	.151	.784	.562	1.093
Radiation(2)	-.359	.479	.561	1	.454	.698	.273	1.786
Radiation(3)	-.266	.306	.753	1	.386	.767	.421	1.397
Radiation(4)	.532	.610	.762	1	.383	1.703	.515	5.625
RadSurgCombine	-.100	.606	.027	1	.869	.905	.276	2.970
SurgCombinary	.174	.573	.092	1	.762	1.190	.387	3.656
PctNonHSGrad	-.070	.116	.365	1	.546	.932	.743	1.170
PctHSonly	-.083	.116	.511	1	.475	.920	.733	1.156

PctSomeColl	-.063	.117	.291	1	.589	.939	.747	1.180
Pct4yrColl	-.068	.117	.339	1	.560	.934	.744	1.174
MedIncome	.000	.000	.005	1	.945	1.000	1.000	1.000
MyoInfarc	1.407	2.546	.306	1	.580	4.085	.028	600.147
OldMyoInfarc	-3.056	13.031	.055	1	.815	.047	.000	5.825E9
CHF	-19.92	10810.1	.000	1	.999	.000	.000	.
PeriphVascDis	1.392	1.151	1.46	1	.226	4.025	.421	38.437
CerebroVascDis	-.565	1.949	.084	1	.772	.568	.012	25.932
COPD	.403	.523	.594	1	.441	1.496	.537	4.172
Paralysis	-45.11	102272	.000	1	1.00	.000	.000	.
Diabetes	-.831	1.243	.447	1	.504	.436	.038	4.980
DiabetesSequelae	2.792	.958	8.49	1	.004	16.321	2.497	106.681
Rheum	-2.447	8.137	.090	1	.764	.087	.000	730957.2
Constant	2.531	11.699	.047	1	.829	12.568		

a. Variable(s) entered on step 1: sPSA, Race, Age, Grade, MarStatus, Radiation, RadSurgCombinary, SurgCombinary, PctNonHSGrad, PctHSonly, PctSomeColl, Pct4yrColl, MedIncome, MyoInfarc, OldMyoInfarc, CHF, PeriphVascDisDx, CerebroVascDis, COPD, Paralysis, Diabetes, DiabetesSequelae, Rheum.

Conditional Cox Regression for Quintile 4

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	234	3.0%
	Censored	131	1.7%
	Total	365	4.6%
Cases dropped	Cases with missing values	0	.0%
	Cases with negative time	0	.0%
	Censored cases before the earliest event in a stratum	7535	95.4%
	Total	7535	95.4%
Total		7900	100.0%

a. Dependent Variable: Survival time recode (total # of months)

Categorical Variable Codings[b,c,d,e,f]							
		Frequency	(1)	(2)	(3)	(4)	(5)
Age[a]	14	372	0	0	0	0	
	15	3491	1	0	0	0	
	16	2452	0	1	0	0	
	17	1331	0	0	1	0	
	18	254	0	0	0	1	
Grade[a]	1	431	0				
	2	7469	1				
MarStatus[a]	1	474	0	0	0	0	0
	2	5316	1	0	0	0	0
	3	25	0	1	0	0	0
	4	260	0	0	1	0	0
	5	764	0	0	0	1	0
	9	1061	0	0	0	0	1
Race[a]	1	7819	0				
	2	81	1				
Radiation[a]	0	3960	0	0	0	0	
	1	2467	1	0	0	0	
	2	827	0	1	0	0	
	4	595	0	0	1	0	
	9	51	0	0	0	1	
a. Indicator Parameter Coding							
b. Category variable: Age (Age at Diagnosis Year 1)							
c. Category variable: Grade (Grade 1)							
d. Category variable: MarStatus (Marital Status)							
e. Category variable: Race (SEER Race Recode B)							
f. Category variable: Radiation (Radiation 1)							

Block 0: Beginning Block

Omnibus Tests of Model Coefficients
-2 Log Likelihood
185.763

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]									
-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
	Chi-square	df	Sig.	Chi-square	Df	Sig.	Chi-square	df	Sig.
118.969	52.081	32	.014	66.795	32	.000	66.795	32	.000
a. Beginning Block Number 1. Method = Enter									

Variables in the Equation								
	B	SE	Wald	Df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
sPSA	.646	.891	.526	1	.468	1.909	.333	10.943
Race	-9.76	71.167	.019	1	.891	.000	.000	2.180E56
Age			.957	4	.916			
Age(1)	4.112	14.620	.079	1	.779	61.086	.000	1.701E14
Age(2)	4.294	15.370	.078	1	.780	73.239	.000	8.870E14
Age(3)	3.267	12.763	.066	1	.798	26.223	.000	1.918E12
Age(4)	2.728	8.495	.103	1	.748	15.302	.000	2.604E8
Grade	2.223	3.621	.377	1	.539	9.233	.008	11154.357
HistStageCombine			.	0[a]	.			
MarStatus			1.922	5	.860			
MarStatus(1)	-1.40	5.294	.071	1	.790	.245	.000	7850.527
MarStatus(2)	-2.62	2.637	.989	1	.320	.073	.000	12.752
MarStatus(3)	-1.43	2.456	.341	1	.559	.238	.002	29.338
MarStatus(4)	-1.75	3.478	.253	1	.615	.174	.000	158.564
MarStatus(5)	-1.54	2.962	.272	1	.602	.213	.001	70.839
Radiation			6.317	4	.177			
Radiation(1)	-1.05	.760	1.928	1	.165	.348	.079	1.543
Radiation(2)	-.348	5.854	.004	1	.953	.706	.000	67824.379
Radiation(3)	-.308	1.354	.052	1	.820	.735	.052	10.435
Radiation(4)	8.636	53.845	.026	1	.873	5629.86	.000	3.832E49
RadSurgCombine	3.391	2.518	1.814	1	.178	29.693	.214	4126.941
SurgCombinary	-4.59	9.681	.226	1	.635	.010	.000	1751416.2
Hormones			.	0[a]	.			

PctNonHSGrad	.073	.289	.064	1	.800	1.076	.611	1.896
PctHSonly	.058	.287	.041	1	.839	1.060	.604	1.861
PctSomeColl	.136	.364	.139	1	.709	1.145	.562	2.336
Pct4yrColl	.146	.358	.167	1	.683	1.157	.574	2.333
MedIncome	.000	.000	.269	1	.604	1.000	1.000	1.000
MyoInfarc	-4.68	582.25	.000	1	.994	.009	.000	.
OldMyoInfarc	-63.73	120.02	.282	1	.595	.000	.000	3.043E74
CHF	-10.826	114.79	.009	1	.925	.000	.000	1.025E93
PeriphVascDis	1.964	9.777	.040	1	.841	7.128	.000	1.496E9
CerebroVascDis	-9.506	19.188	.245	1	.620	.000	.000	1.601E12
COPD	-1.674	7.350	.052	1	.820	.187	.000	338148.89
Dementia			.	0[a]	.			
Paralysis			.	0[a]	.			
Diabetes	1.456	5.046	.083	1	.773	4.291	.000	84735.501
DiabetesSequelae	23.763	74.344	.102	1	.749	2.091E10	.000	3.997E73
ChronicRenalFail			.	0[a]	.			
Rheum	-16.086	35.617	.204	1	.652	.000	.000	2.142E23
a. Degree of freedom reduced because of constant or linearly dependent covariates								

Appendix G

Logistic and Conditional Cox Regression Output with Propensity Analysis

Quintile 5

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	11002	100.0
	Missing Cases	0	.0
	Total	11002	100.0
Unselected Cases		0	.0
Total		11002	100.0

a. If weight is in effect, see classification table for the total number of cases.

b. The variable HistStageCombinary is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

c. The variable Hormones is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

d. The variable DEMENTIA (1) is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

e. The variable PARALYSIS (1) is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

f. The variable CHRONIC RENAL FAILURE (2) is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

Dependent Variable Encoding

Original Value	Internal Value
0	0
1	1

Categorical Variables Codings

			Parameter coding				
		Frequency	(1)	(2)	(3)	(4)	(5)
Marital Status	1	312	.000	.000	.000	.000	.000
	2	8609	1.000	.000	.000	.000	.000
	3	17	.000	1.000	.000	.000	.000
	4	264	.000	.000	1.000	.000	.000
	5	817	.000	.000	.000	1.000	.000
	9	983	.000	.000	.000	.000	1.000
Radiation 1	0	4150	.000	.000	.000	.000	
	1	4101	1.000	.000	.000	.000	
	2	1655	.000	1.000	.000	.000	
	4	1070	.000	.000	1.000	.000	
	9	26	.000	.000	.000	1.000	
Age at Diagnosis Year	14	16	.000	.000	.000	.000	
1	15	5386	1.000	.000	.000	.000	
	16	4219	.000	1.000	.000	.000	
	17	1331	.000	.000	1.000	.000	
	18	50	.000	.000	.000	1.000	
Grade 1	1	314	.000				
	2	10688	1.000				
SEER Race Recode B	1	10994	.000				
	2	8	1.000				

Block 0: Beginning Block

Classification Table[a,b]

			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 0	Mortality	0	10715	0	100.0
		1	287	0	.0
	Overall Percentage				97.4

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	Df	Sig.	Exp(B)
Step 0	Constant	-3.620	.060	3662.687	1	.000	.027

Variables not in the Equation[a]

		Score	df	Sig.
Step 0	sPSA	.433	1	.511
	Race	.214	1	.643
	Age	18.443	4	.001
	Age(1)	16.067	1	.000
	Age(2)	6.018	1	.014
	Age(3)	6.860	1	.009
	Age(4)	.073	1	.787
	Grade	.619	1	.431
	MarStatus	21.862	5	.001
	MarStatus(1)	7.253	1	.007
	MarStatus(2)	.456	1	.499
	MarStatus(3)	.682	1	.409
	MarStatus(4)	.968	1	.325
	MarStatus(5)	20.057	1	.000
	Radiation	35.031	4	.000
	Radiation(1)	4.411	1	.036
	Radiation(2)	13.763	1	.000
	Radiation(3)	.983	1	.321
	Radiation(4)	.698	1	.403

RadSurgCombinary	.004	1	.950
SurgCombinary	.170	1	.680
PctNonHSGrad	2.620	1	.106
PctHSonly	4.789	1	.029
PctSomeColl	.246	1	.620
Pct4yrColl	3.261	1	.071
MedIncome	.519	1	.471
MyoInfarc	.000	1	.990
OldMyoInfarc	.940	1	.332
CHF	.080	1	.777
PeriphVascDis	2.497	1	.114
CerebroVascDis	.149	1	.700
COPD	.050	1	.823
Diabetes	.306	1	.580
DiabetesSequelae	1.005	1	.316
Rheum	.627	1	.428

a. Residual Chi-Squares are not computed because of redundancies.

Block 1: Method = Enter

Omnibus Tests of Model Coefficients

		Chi-square	Df	Sig.
Step 1	Step	73.311	32	.000
	Block	73.311	32	.000
	Model	73.311	32	.000

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	2586.141[a]	.007	.031

a. Estimation terminated at iteration number 20 because maximum iterations have been reached. Final solution cannot be found.

Classification Table[a]					
			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 1	Mortality	0	10715	0	100.0
		1	287	0	.0
	Overall Percentage				97.4
a. The cut value is .500					

Variables in the Equation								
							95% C.I. for Exp(B)	
	B	S.E.	Wald	Df	Sig.	Exp(B)	Lower	Upper
sPSA	-.086	.143	.358	1	.549	.918	.693	1.215
Race	-16.44	14180	.000	1	.999	.000	.000	.
Age			11.403	4	.022			
Age(1)	16.116	10040	.000	1	.999	9982633	.000	.
Age(2)	16.474	10040	.000	1	.999	1.427E7	.000	.
Age(3)	16.664	10040	.000	1	.999	1.726E7	.000	.
Age(4)	16.242	10040	.000	1	.999	1.132E7	.000	.
Grade	.184	.436	.178	1	.673	1.202	.512	2.823
MarStatus			14.763	5	.011			
MarStatus(1)	-.346	.405	.728	1	.393	.708	.320	1.566
MarStatus(2)	-17.67	9676	.000	1	.999	.000	.000	.
MarStatus(3)	.213	.500	.181	1	.670	1.237	.465	3.295
MarStatus(4)	-.473	.452	1.095	1	.295	.623	.257	1.512
MarStatus(5)	.314	.404	.605	1	.437	1.369	.621	3.019
Radiation			20.496	4	.000			
Radiation(1)	-.451	.142	10.094	1	.001	.637	.482	.841
Radiation(2)	-1.199	.305	15.483	1	.000	.302	.166	.548
Radiation(3)	-.421	.235	3.217	1	.073	.656	.414	1.040
Radiation(4)	-18.03	7820.6	.000	1	.998	.000	.000	.
RadSurgCombine	.418	.596	.492	1	.483	1.519	.472	4.888
SurgCombinary	.484	.802	.364	1	.546	1.622	.337	7.817
PctNonHSGrad	.055	.102	.289	1	.591	1.056	.865	1.289
PctHSonly	.056	.102	.304	1	.581	1.058	.866	1.292

PctSomeColl	.044	.102	.182	1	.670	1.044	.855	1.276
Pct4yrColl	.049	.102	.228	1	.633	1.050	.860	1.282
MedIncome	.000	.000	.148	1	.701	1.000	1.000	1.000
MyoInfarc	.275	2.989	.008	1	.927	1.317	.004	461.590
OldMyoInfarc	-312.4	124736	.000	1	.998	.000	.000	.
CHF	-18.87	26481	.000	1	.999	.000	.000	.
PeriphVascDis	2.557	1.334	3.674	1	.055	12.892	.944	176.079
CerebroVascDis	.842	2.317	.132	1	.716	2.320	.025	217.574
COPD	.802	.566	2.006	1	.157	2.230	.735	6.766
Diabetes	1.338	1.064	1.582	1	.208	3.813	.474	30.686
DiabetesSequelae	-2.871	2.328	1.521	1	.217	.057	.001	5.427
Rheum	-6.958	11.153	.389	1	.533	.001	.000	2960889
Constant	-8.403	17375	.000	1	1.00	.000		

a. Variable(s) entered on step 1: sPSA, Race, Age, Grade, MarStatus, Radiation, RadSurgCombinary, SurgCombinary, PctNonHSGrad, PctHSonly, PctSomeColl, Pct4yrColl, MedIncome, MyoInfarc, OldMyoInfarc, CHF, PeriphVascDisDx, CerebroVascDis, COPD, Diabetes, DiabetesSequelae, Rheum.

Conditional Cox Regression for Quintile 5

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	287	2.6%
	Censored	161	1.5%
	Total	448	4.1%
Cases dropped	Cases with missing values	0	.0%
	Cases with negative time	0	.0%
	Censored cases before the earliest event in a stratum	10554	95.9%
	Total	10554	95.9%
Total		11002	100.0%

a. Dependent Variable: Survival time recode (total # of months)

Categorical Variable Codings[b,c,d,e,f]

		Frequency	(1)	(2)	(3)	(4)	(5)
Age[a]	14	16	0	0	0	0	
	15	5386	1	0	0	0	
	16	4219	0	1	0	0	
	17	1331	0	0	1	0	
	18	50	0	0	0	1	
Grade[a]	1	314	0				
	2	10688	1				
MarStatus[a]	1	312	0	0	0	0	0
	2	8609	1	0	0	0	0
	3	17	0	1	0	0	0
	4	264	0	0	1	0	0
	5	817	0	0	0	1	0
	9	983	0	0	0	0	1
Race[a]	1	10994	0				
	2	8	1				
Radiation[a]	0	4150	0	0	0	0	
	1	4101	1	0	0	0	
	2	1655	0	1	0	0	
	4	1070	0	0	1	0	
	9	26	0	0	0	1	

a. Indicator Parameter Coding
b. Category variable: Age (Age at Diagnosis Year 1)
c. Category variable: Grade (Grade 1)
d. Category variable: MarStatus (Marital Status)
e. Category variable: Race (SEER Race Recode B)
f. Category variable: Radiation (Radiation 1)

Block 0: Beginning Block

Omnibus Tests of Model Coefficients
-2 Log Likelihood
228.739

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]									
-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
	Chi-square	Df	Sig.	Chi-square	df	Sig.	Chi-square	Df	Sig.
153.41	60.061	26	.000	75.328	26	.000	75.328	26	.000
a. Beginning Block Number 1. Method = Enter									

Variables in the Equation								
	B	SE	Wald	Df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
sPSA	.508	.660	.593	1	.441	1.663	.456	6.066
Race			.	0[a]	.			
Age			7.204	2[a]	.027			
Age(1)	-.417	.782	.284	1	.594	.659	.142	3.051
Age(2)	.575	1.001	.330	1	.565	1.778	.250	12.642
Grade	3.07	1.729	3.154	1	.076	21.573	.727	639.751
HistStageCombine			.	0[a]	.			
MarStatus			1.129	5	.951			
MarStatus(1)	.164	1.768	.009	1	.926	1.179	.037	37.697
MarStatus(2)	-13.3	270.8	.002	1	.961	.000	.000	5.476E224
MarStatus(3)	11.19	98.69	.013	1	.910	72549.77	.000	7.346E88
MarStatus(4)	-.441	1.462	.091	1	.763	.643	.037	11.297
MarStatus(5)	-.377	1.322	.081	1	.775	.686	.051	9.157
Radiation			13.059	3[a]	.005			
Radiation(1)	-1.474	.416	12.538	1	.000	.229	.101	.518
Radiation(2)	-1.147	1.833	.392	1	.531	.318	.009	11.532
Radiation(3)	-1.076	.597	3.246	1	.072	.341	.106	1.099
RadSurgCombine	.961	1.811	.281	1	.596	2.613	.075	91.017
SurgCombinary	-.801	3.467	.053	1	.817	.449	.001	401.450
Hormones			.	0[a]	.			
PctNonHSGrad	.593	.284	4.348	1	.037	1.809	1.036	3.157

PctHSonly	.599	.289	4.287	1	.038	1.819	1.032	3.206
PctSomeColl	.667	.295	5.093	1	.024	1.948	1.092	3.476
Pct4yrColl	.672	.294	5.205	1	.023	1.958	1.099	3.486
MedIncome	.000	.000	2.643	1	.104	1.000	1.000	1.000
MyoInfarc	-4.472	7.439	.361	1	.548	.011	.000	24557.688
OldMyoInfarc			.	0[a]	.			
CHF			.	0[a]	.			
PeriphVascDis	3.047	4.529	.452	1	.501	21.042	.003	150729.64
CerebroVascDis	-8.363	9.210	.825	1	.364	.000	.000	16124.160
COPD	-1.683	2.572	.428	1	.513	.186	.001	28.718
Dementia			.	0[a]	.			
Paralysis			.	0[a]	.			
Diabetes	4.433	3.177	1.947	1	.163	84.194	.166	42624.670
DiabetesSequelae	-24.81	434.3	.003	1	.954	.000	.000	.
ChronicRenalFail			.	0[a]	.			
Rheum	-151.6	2976	.003	1	.959	.000	.000	.
a. Degree of freedom reduced because of constant or linearly dependent covariates								

Appendix H

Logistic and Conditional Cox Regression with Propensity Analysis

AGE Quartile 1

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	9392	100.0
	Missing Cases	0	.0
	Total	9392	100.0
Unselected Cases		0	.0
Total		9392	100.0

a. If weight is in effect, see classification table for the total number of cases.

b. The variable Hormones is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

Dependent Variable Encoding

Original Value	Internal Value
0	0
1	1

Categorical Variables Codings

			Parameter coding				
		Frequency	(1)	(2)	(3)	(4)	(5)
Marital Status	1	739	.000	.000	.000	.000	.000
	2	7178	1.000	.000	.000	.000	.000
	3	41	.000	1.000	.000	.000	.000
	4	432	.000	.000	1.000	.000	.000
	5	343	.000	.000	.000	1.000	.000
	9	659	.000	.000	.000	.000	1.000

Radiation 1	0	5994	.000	.000	.000	.000
	1	1863	1.000	.000	.000	.000
	2	792	.000	1.000	.000	.000
	4	619	.000	.000	1.000	.000
	9	124	.000	.000	.000	1.000
Grade 1	1	527	.000			
	2	8865	1.000			
SEER Race Recode	1	8241	.000			
	2	1151	1.000			

Block 0: Beginning Block

Classification Table[a,b]

			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 0	Mortality	0	9214	0	100.0
		1	178	0	.0
	Overall Percentage				98.1

a. Constant is included in the model.
b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-3.947	.076	2720.053	1	.000	.019

Variables not in the Equation[a]

		Score	Df	Sig.
Step 0	sPSA	.206	1	.650
	Grade(1)	.438	1	.508
	HistStageCombine	22.340	1	.000
	MarStatus	13.151	5	.022
	MarStatus(1)	6.265	1	.012
	MarStatus(2)	1.971	1	.160
	MarStatus(3)	.005	1	.946

MarStatus(4)	.041	1	.840
MarStatus(5)	9.696	1	.002
Race(1)	.075	1	.784
Radiation	1.158	1	.282
RadSurgCombined	7.521	1	.006
SurgCombinary	9.199	1	.002
PctNonHSGrad	.003	1	.953
PctHSonly	.699	1	.403
PctSomeColl	6.224	1	.013
Pct4yrColl	2.189	1	.139
MedIncome	1.129	1	.288
MyoInfarc	.170	1	.680
OldMyoInfarc	.071	1	.790
CHF	.175	1	.676
PeriphVascDis	2.823	1	.093
CerebroVascDis	1.823	1	.177
COPD	.703	1	.402
Dementia	3.537	1	.060
Paralysis	.271	1	.603
Diabetes	.010	1	.920
DiabetesSequelae	2.567	1	.109
ChronicRenalFail	.854	1	.355
Rheum	2.702	1	.100

a. Residual Chi-Squares are not computed because of redundancies.

Block 1: Method = Enter

Omnibus Tests of Model Coefficients

		Chi-square	Df	Sig.
Step 1	Step	76.269	31	.000
	Block	76.269	31	.000
	Model	76.269	31	.000

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	1698.702[a]	.007	.041

a. Estimation terminated at iteration number 20 because maximum iterations have been reached. Final solution cannot be found.

Hosmer and Lemeshow Test

Step	Chi-square	Df	Sig.
1	5.686	8	.682

Classification Table[a]

			Predicted Mortality		
	Observed		0	1	Percentage Correct
Step 1	Mortality	0	9214	0	100.0
		1	178	0	.0
	Overall Percentage				98.1

a. The cut value is .500

Variables in the Equation

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for Exp(B) Lower	Upper
sPSA	-.086	.153	.320	1	.572	.917	.680	1.237
Race(1)	.129	.249	.268	1	.605	1.138	.698	1.855
Grade(1)	-.071	.309	.053	1	.819	.932	.509	1.706
HistStageCombine	-1.451	.369	15.457	1	.000	.234	.114	.483
MarStatus			14.971	5	.010			
MarStatus(1)	-.323	.268	1.448	1	.229	.724	.428	1.225
MarStatus(2)	.651	.801	.660	1	.417	1.918	.399	9.226
MarStatus(3)	-.155	.437	.126	1	.722	.856	.363	2.017
MarStatus(4)	-.316	.485	.427	1	.514	.729	.282	1.884
MarStatus(5)	.587	.339	2.993	1	.084	1.799	.925	3.497

Radiation			11.715	4	.020			
Radiation(1)	.699	.208	11.345	1	.001	2.013	1.340	3.023
Radiation(2)	.514	.315	2.666	1	.103	1.671	.902	3.096
Radiation(3)	.330	.354	.872	1	.350	1.392	.696	2.784
Radiation(4)	.044	.558	.006	1	.938	1.045	.350	3.117
RadSurgCombine	.226	.346	.424	1	.515	1.253	.636	2.470
SurgCombinary	.730	.191	14.592	1	.000	2.076	1.427	3.019
PctNonHSGrad	-.004	.011	.117	1	.733	.996	.975	1.018
PctHSonly	-.001	.010	.008	1	.930	.999	.980	1.019
PctSomeColl	-.030	.014	4.683	1	.030	.970	.944	.997
MedIncome	.000	.000	.118	1	.732	1.000	1.000	1.000
MyoInfarc	-.932	4.305	.047	1	.829	.394	.000	1817.095
OldMyoInfarc	-3.599	13.82	.068	1	.795	.027	.000	1.599E10
CHF	-.164	.840	.038	1	.845	.848	.163	4.405
PeriphVascDisDx	2.483	1.347	3.396	1	.065	11.975	.854	167.886
CerebroVascDis	-4.037	2.777	2.112	1	.146	.018	.000	4.083
COPD	-.412	.483	.729	1	.393	.662	.257	1.706
Dementia	3.059	1.503	4.140	1	.042	21.300	1.119	405.462
Paralysis	-40.21	2524	.000	1	.999	.000	.000	.
Diabetes	.806	1.256	.412	1	.521	2.239	.191	26.254
DiabetesSequelae	-39.58	7572	.000	1	.996	.000	.000	.
ChronicRenalFail	-24.76	8528	.000	1	.998	.000	.000	.
Rheum	11.182	6.685	2.799	1	.094	71857	.147	3.519E10
Constant	-2.058	.950	4.693	1	.030	.128		

a. Variable(s) entered on step 1: sPSA, Race, Grade, HistStageCombinary, MarStatus, Radiation, RadSurgCombinary, SurgCombinary, PctNonHSGrad, PctHSonly, PctSomeColl, MedIncome, MyoInfarc, OldMyoInfarc, CHF, PeriphVascDisDx, CerebroVascDis, COPD, Dementia, Paralysis, Diabetes, DiabetesSequelae, ChronicRenalFail, Rheum.

Conditional Cox Regression for AGE Quartile 1

Case Processing Summary			
		N	Percent
Cases available in analysis	Event[a]	178	1.9%
	Censored	101	1.1%
	Total	279	3.0%
Cases dropped	Cases with missing values	0	.0%
	Cases with negative time	0	.0%
	Censored cases before the earliest event in a stratum	9113	97.0%
	Total	9113	97.0%
Total		9392	100.0%

a. Dependent Variable: Survival time recode (total # of months)

Categorical Variable Codings[b,c,d,e]							
		Frequency	(1)	(2)	(3)	(4)	(5)
Grade[a]	1	527	0				
	2	8865	1				
MarStatus[a]	1	739	0	0	0	0	0
	2	7178	1	0	0	0	0
	3	41	0	1	0	0	0
	4	432	0	0	1	0	0
	5	343	0	0	0	1	0
	9	659	0	0	0	0	1
Race[a]	1	8241	0				
	2	1151	1				
Radiation[a]	0	5994	0	0	0	0	
	1	1863	1	0	0	0	
	2	792	0	1	0	0	
	4	619	0	0	1	0	
	9	124	0	0	0	1	

a. Indicator Parameter Coding

b. Category variable: Grade (Grade 1)
c. Category variable: MarStatus (Marital Status)
d. Category variable: Race (SEER Race Recode B)
e. Category variable: Radiation (Radiation 1)

Block 0: Beginning Block

Omnibus Tests of Model Coefficients
-2 Log Likelihood
140.016

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]

-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
	Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
104.759	28.023	26	.357	35.257	26	.106	35.257	26	.106

a. Beginning Block Number 1. Method = Enter

b.

Variables in the Equation

	B	SE	Wald	Df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
sPSA	-.127	.271	.221	1	.639	.880	.518	1.498
Race	.968	16.701	.003	1	.954	2.633	.000	4.327E14
Grade	.522	5.601	.009	1	.926	1.685	.000	98724.527
HistStageCombine			.	0[a]	.			
MarStatus			.883	5	.971			
MarStatus(1)	-.466	7.998	.003	1	.954	.627	.000	4034013.4
MarStatus(2)	5.520	95.537	.003	1	.954	249.604	.000	5.229E83
MarStatus(3)	-.845	3.136	.073	1	.788	.430	.001	200.889

MarStatus(4)	-8.461	42.783	.039	1	.843	.000	.000	5.533E32
MarStatus(5)	-.123	4.328	.001	1	.977	.884	.000	4270.416
Radiation			1.919	4	.751			
Radiation(1)	.002	1.251	.000	1	.999	1.002	.086	11.629
Radiation(2)	-.846	9.066	.009	1	.926	.429	.000	2.234E7
Radiation(3)	-1.345	2.356	.326	1	.568	.260	.003	26.386
Radiation(4)	32.06	112.81	.081	1	.776	8.417E13	.000	8.956E109
RadSurgCombine	1.558	2.041	.583	1	.445	4.750	.087	259.594
SurgCombinary	-1.470	15.321	.009	1	.924	.230	.000	2.530E12
Hormones			.	0[a]	.			
PctNonHSGrad	-.027	.311	.008	1	.930	.973	.529	1.789
PctHSonly	-.001	.421	.000	1	.998	.999	.438	2.280
PctSomeColl	-.085	.054	2.525	1	.112	.918	.827	1.020
MedIncome	.000	.000	.023	1	.880	1.000	1.00	1.000
OldMyoInfarc	296.77	1593.9	.035	1	.852	7.737E128	.000	.
CHF	10.128	72.182	.020	1	.888	25043.890	.000	6.926E65
PeriphVascDisDx	20.389	119.40	.029	1	.864	7.157E8	.000	3.120E110
CerebroVascDis	2.818	279.89	.000	1	.992	16.747	.000	2.932E239
COPD	-.288	11.961	.001	1	.981	.750	.000	1.138E10
Dementia			.	0[a]	.			
Paralysis			.	0[a]	.			
Diabetes	1.734	7.609	.052	1	.820	5.665	.000	1.696E7
DiabetesSequelae			.	0[a]	.			
ChronicRenalFail	-22.99	118.25	.038	1	.846	.000	.000	4.708E90
Rheum	81.023	463.25	.031	1	.861	1.542E35	.000	.
a. Degree of freedom reduced because of constant or linearly dependent covariates								

Appendix I

Logistic and Conditional Cox Regression with Propensity Analysis

AGE Quartile 2

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	7058	100.0
	Missing Cases	0	.0
	Total	7058	100.0
Unselected Cases		0	.0
Total		7058	100.0

a. If weight is in effect, see classification table for the total number of cases.

b. The variable Hormones is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

Dependent Variable Encoding

Original Value	Internal Value
0	0
1	1

Categorical Variables Codings

			Parameter coding				
		Frequency	(1)	(2)	(3)	(4)	(5)
Marital Status	1	407	.000	.000	.000	.000	.000
	2	5290	1.000	.000	.000	.000	.000
	3	22	.000	1.000	.000	.000	.000
	4	273	.000	.000	1.000	.000	.000
	5	457	.000	.000	.000	1.000	.000

	9	609	.000	.000	.000	.000	1.000
Radiation 1	0	3275	.000	.000	.000	.000	
	1	2405	1.000	.000	.000	.000	
	2	710	.000	1.000	.000	.000	
	4	607	.000	.000	1.000	.000	
	9	61	.000	.000	.000	1.000	
Grade 1	1	423	.000				
	2	6635	1.000				
SEER Race Recode	1	6594	.000				
	2	464	1.000				

Block 0: Beginning Block

Classification Table[a,b]

			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 0	Mortality	0	6881	0	100.0
		1	177	0	.0
	Overall Percentage				97.5

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-3.660	.076	2312.028	1	.000	.026

Variables not in the Equation[a]

		Score	Df	Sig.
Step 0	sPSA	.979	1	.322
	Grade(1)	.589	1	.443
	HistStageCombinary	27.379	1	.000
	MarStatus	8.789	5	.118
	MarStatus(1)	.055	1	.814
	MarStatus(2)	.568	1	.451

MarStatus(3)	3.660	1	.056
MarStatus(4)	.204	1	.651
MarStatus(5)	4.389	1	.036
Race(1)	1.797	1	.180
Radiation	.090	1	.764
RadSurgCombinary	1.432	1	.231
PctNonHSGrad	3.714	1	.054
PctHSonly	6.333	1	.012
PctSomeColl	.013	1	.911
Pct4yrColl	6.839	1	.009
MedIncome	4.316	1	.038
MyoInfarc	.003	1	.954
OldMyoInfarc	.791	1	.374
CHF	.543	1	.461
PeriphVascDisDx	.460	1	.497
CerebroVascDis	.001	1	.978
COPD	.039	1	.844
Dementia	38.881	1	.000
Paralysis	6.262	1	.012
Diabetes	.021	1	.884
DiabetesSequelae	.005	1	.945
ChronicRenalFail	1.233	1	.267
Rheum	1.609	1	.205

. Residual Chi-Squares are not computed because of redundancies.

Block 1: Method = Enter

Omnibus Tests of Model Coefficients

		Chi-square	Df	Sig.
Step 1	Step	80.852	32	.000
	Block	80.852	32	.000
	Model	80.852	32	.000

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	1573.433[a]	.011	.055

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	1573.433[a]	.011	.055

a. Estimation terminated at iteration number 20 because maximum iterations have been reached. Final solution cannot be found.

Classification Table[a]

			Predicted Mortality		Percentage Correct
	Observed		0	1	
Step 1	Mortality	0	6881	0	100.0
		1	176	1	.6
	Overall Percentage				97.5

a. The cut value is .500

Variables in the Equation

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for Exp(B) Lower	Upper
sPSA	-.143	.155	.846	1	.358	.867	.639	1.175
Race(1)	.594	.290	4.199	1	.055	1.811	1.026	3.195
Grade(1)	-.179	.299	.361	1	.548	.836	.465	1.501
HistStageCombine	-1.280	.399	10.28	1	.001	.278	.127	.608
MarStatus			11.69	5	.039			
MarStatus(1)	.154	.373	.171	1	.679	1.167	.562	2.425
MarStatus(2)	-17.283	8452	.000	1	.998	.000	.000	.
MarStatus(3)	-1.027	.797	1.660	1	.198	.358	.075	1.708
MarStatus(4)	.023	.495	.002	1	.963	1.023	.388	2.700
MarStatus(5)	.820	.423	3.760	1	.052	2.271	.991	5.203
Radiation			18.371	4	.001			
Radiation(1)	.637	.185	11.855	1	.001	1.891	1.316	2.718
Radiation(2)	-.277	.389	.505	1	.477	.758	.353	1.627
Radiation(3)	.756	.279	7.327	1	.007	2.130	1.232	3.683

Radiation(4)	-.604	1.03	.342	1	.559	.546	.072	4.144
RadSurgCombine	-.144	.394	.133	1	.715	.866	.400	1.875
SurgCombinary	.742	.180	17.060	1	.000	2.099	1.477	2.985
PctNonHSGrad	-.138	.132	1.088	1	.297	.871	.672	1.129
PctHSonly	-.142	.133	1.139	1	.286	.867	.668	1.126
PctSomeColl	-.136	.133	1.043	1	.307	.873	.673	1.133
Pct4yrColl	-.133	.133	1.013	1	.314	.875	.675	1.135
MedIncome	.000	.000	.157	1	.692	1.000	1.000	1.000
MyoInfarc	.739	3.07	.058	1	.810	2.094	.005	863.99
OldMyoInfarc	-14.450	19.1	.567	1	.451	.000	.000	1.126E10
CHF	-1.068	1.27	.699	1	.403	.344	.028	4.201
PeriphVascDisDx	-1.385	2.07	.448	1	.503	.250	.004	14.456
CerebroVascDis	-.447	1.90	.055	1	.815	.640	.015	26.776
COPD	.225	.400	.318	1	.573	1.253	.572	2.742
Dementia	30.234	5172	.000	1	1.000	1.351E13	.000	.
Paralysis	6.488	3.25	3.978	1	.046	657.409	1.119	38621
Diabetes	-.250	1.34	.035	1	.852	.779	.056	10.870
DiabetesSequelae	.196	1.73	.013	1	.910	1.217	.040	36.583
ChronicRenalFail	1.714	1.58	1.173	1	.279	5.550	.250	123.34
Rheum	-191.92	5420	.000	1	.997	.000	.000	.
Constant	10.608	13.2	.639	1	.424	40443.3		

a. Variable(s) entered on step 1: sPSA, Race, Grade, HistStageCombinary, MarStatus, Radiation, RadSurgCombinary, SurgCombinary, PctNonHSGrad, PctHSonly, PctSomeColl, Pct4yrColl, MedIncome, MyoInfarc, OldMyoInfarc, CHF, PeriphVascDisDx, CerebroVascDis, COPD, Dementia, Paralysis, Diabetes, DiabetesSequelae, ChronicRenalFail, Rheum.

Conditional Cox Regression for AGE Quartile 2

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	177	2.5%
	Censored	96	1.4%
	Total	273	3.9%
Cases dropped	Cases with missing values	0	.0%

	Cases with negative time	0	.0%
	Censored cases before the earliest event in a stratum	6785	96.1%
	Total	6785	96.1%
Total		7058	100.0%

a. Dependent Variable: Survival time recode (total # of months)

Categorical Variable Codings[b,c,d,e]

		Frequency	(1)	(2)	(3)	(4)	(5)
Grade[a]	1	423	0				
	2	6635	1				
MarStatus[a]	1	407	0	0	0	0	0
	2	5290	1	0	0	0	0
	3	22	0	1	0	0	0
	4	273	0	0	1	0	0
	5	457	0	0	0	1	0
	9	609	0	0	0	0	1
Race[a]	1	6594	0				
	2	464	1				
Radiation[a]	0	3275	0	0	0	0	
	1	2405	1	0	0	0	
	2	710	0	1	0	0	
	4	607	0	0	1	0	
	9	61	0	0	0	1	

a. Indicator Parameter Coding
b. Category variable: Grade (Grade 1)
c. Category variable: MarStatus (Marital Status)
d. Category variable: Race (SEER Race Recode B)
e. Category variable: Radiation (Radiation 1)

Block 0: Beginning Block

Omnibus Tests of Model Coefficients
-2 Log Likelihood
137.243

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]

	Overall (score)			Change From Previous Step			Change From Previous Block		
-2 Log Likelihood	Chi-square	Df	Sig.	Chi-square	Df	Sig.	Chi-square	df	Sig.
103.040	26.109	26	.457	34.203	26	.130	34.203	26	.130

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
sPSA	-.115	.347	.109	1	.741	.891	.451	1.761
Race	4.905	3.671	1.785	1	.182	134.963	.101	179945.410
Grade	-.378	1.195	.100	1	.752	.685	.066	7.130
HistStageCombine			.	0[a]	.			
MarStatus			2.478	4[a]	.649			
MarStatus(1)	-.636	1.569	.164	1	.685	.530	.024	11.463
MarStatus(3)	.751	2.095	.128	1	.720	2.119	.035	128.552
MarStatus(4)	-.707	1.225	.334	1	.564	.493	.045	5.435
MarStatus(5)	.429	1.230	.121	1	.728	1.535	.138	17.103
Radiation			2.971	3[a]	.396			
Radiation(1)	.138	.547	.064	1	.801	1.148	.393	3.358
Radiation(2)	-2.512	1.821	1.902	1	.168	.081	.002	2.880
Radiation(3)	-.223	.778	.082	1	.774	.800	.174	3.673
RadSurgCombine	2.992	1.768	2.865	1	.091	19.930	.623	637.309

SurgCombinary	.370	2.586	.020	1	.886	1.448	.009	229.914
Hormones			.	0[a]	.			
PctNonHSGrad	.434	.375	1.338	1	.247	1.544	.740	3.222
PctHSonly	.425	.383	1.231	1	.267	1.530	.722	3.243
PctSomeColl	.420	.385	1.194	1	.274	1.522	.716	3.235
Pct4yrColl	.384	.384	.999	1	.318	1.468	.691	3.117
MedIncome	.000	.000	1.276	1	.259	1.000	1.000	1.000
MyoInfarc			.	0[a]	.			
OldMyoInfarc	-185.6	1378.9	.018	1	.893	.000	.000	.
CHF	4.693	3.991	1.383	1	.240	109.175	.044	272523.863
PeriphVascDisDx	-46.56	457.78	.010	1	.919	.000	.000	.
CerebroVascDis	1.503	7.215	.043	1	.835	4.496	.000	6231774.96
COPD	.389	2.241	.030	1	.862	1.476	.018	119.223
Dementia			.	0[a]	.			
Paralysis	28.686	418.06	.005	1	.945	2.871E1	.000	.
Diabetes	2.900	3.756	.596	1	.440	18.180	.012	28646.852
Rheum	-65.38	1805.3	.001	1	.971	.000	.000	.
a. Degree of freedom reduced because of constant or linearly dependent covariates								

Appendix J

Logistic and Conditional Cox Regression with Propensity Analysis

AGE Quartile 3

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	3118	100.0
	Missing Cases	0	.0
	Total	3118	100.0
Unselected Cases		0	.0
Total		3118	100.0

a. If weight is in effect, see classification table for the total number of cases.

b. The variable Hormones is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

Dependent Variable Encoding

Original Value	Internal Value
0	0
1	1

Categorical Variables Codings

			Parameter coding				
		Frequency	(1)	(2)	(3)	(4)	(5)
Marital Status	1	164	.000	.000	.000	.000	.000
	2	2186	1.000	.000	.000	.000	.000
	3	1	.000	1.000	.000	.000	.000
	4	84	.000	.000	1.000	.000	.000
	5	286	.000	.000	.000	1.000	.000
	9	397	.000	.000	.000	.000	1.000

Radiation 1	0	1456	.000	.000	.000	.000
	1	1133	1.000	.000	.000	.000
	2	279	.000	1.000	.000	.000
	4	224	.000	.000	1.000	.000
	9	26	.000	.000	.000	1.000
Grade 1	1	181	.000			
	2	2937	1.000			
SEER Race Recode	1	2963	.000			
	2	155	1.000			

Block 0: Beginning Block

Classification Table[a,b]

			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 0	Mortality	0	2994	0	100.0
		1	124	0	.0
	Overall Percentage				96.0

a. Constant is included in the model.
b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-3.184	.092	1207.164	1	.000	.041

Variables not in the Equation[a]

		Score	df	Sig.
Step 0	sPSA	.840	1	.359
	Grade(1)	.221	1	.639
	HistStageCombinary	50.731	1	.000
	MarStatus	4.344	5	.501
	MarStatus(1)	1.928	1	.165
	MarStatus(2)	.041	1	.839
	MarStatus(3)	.139	1	.709

MarStatus(4)	3.191	1	.074
MarStatus(5)	.370	1	.543
Race(1)	1.780	1	.182
Radiation	9.068	1	.003
RadSurgCombinary	2.901	1	.089
SurgCombinary	38.416	1	.000
PctNonHSGrad	10.473	1	.001
PctHSonly	9.557	1	.002
PctSomeColl	.694	1	.405
Pct4yrColl	10.993	1	.001
MedIncome	3.817	1	.051
OldMyoInfarc	1.806	1	.179
CHF	1.255	1	.263
PeriphVascDisDx	1.159	1	.282
CerebroVascDis	.652	1	.419
COPD	.081	1	.776
Dementia	.083	1	.773
Paralysis	4.635	1	.031
Diabetes	.052	1	.820
DiabetesSequelae	.311	1	.577
ChronicRenalFail	.249	1	.618
Rheum	.545	1	.461

a. Residual Chi-Squares are not computed because of redundancies.

Block 1: Method = Enter

Omnibus Tests of Model Coefficients

		Chi-square	Df	Sig.
Step 1	Step	88.025	32	.000
	Block	88.025	32	.000
	Model	88.025	32	.000

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	960.505[a]	.026	.092

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	960.505[a]	.026	.092

a. Estimation terminated at iteration number 20 because maximum iterations have been reached. Final solution cannot be found.

Classification Table[a]

			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 1	Mortality	0	2994	0	100.0
		1	123	1	.8
	Overall Percentage				96.1

a. The cut value is .500

Variables in the Equation

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for Exp(B)	
							Lower	Upper
sPSA	-.251	.191	1.731	1	.188	.778	.535	1.131
Race(1)	-.355	.610	.339	1	.561	.701	.212	2.317
Grade(1)	.461	.438	1.110	1	.292	1.585	.673	3.737
HistStageCombine	-2.013	.516	15.233	1	.000	.134	.049	.367
MarStatus			7.145	5	.210			
MarStatus(1)	-.040	.478	.007	1	.933	.961	.376	2.454
MarStatus(2)	-18.905	40192.970	.000	1	1.000	.000	.000	.
MarStatus(3)	.555	.693	.640	1	.424	1.741	.448	6.775
MarStatus(4)	.622	.528	1.391	1	.238	1.863	.662	5.242
MarStatus(5)	.352	.527	.446	1	.504	1.422	.506	3.992
Radiation			8.306	4	.081			
Radiation(1)	-.352	.221	2.541	1	.111	.703	.456	1.084
Radiation(2)	-1.328	.533	6.196	1	.013	.265	.093	.754
Radiation(3)	-.547	.446	1.504	1	.220	.578	.241	1.387
Radiation(4)	-18.388	7519.152	.000	1	.998	.000	.000	.
RadSurgCombine	.586	.531	1.217	1	.270	1.796	.635	5.086

SurgCombinary	.944	.217	18.846	1	.000	2.570	1.678	3.935
PctNonHSGrad	-.095	.159	.356	1	.551	.910	.666	1.242
PctHSonly	-.083	.160	.268	1	.605	.921	.673	1.259
PctSomeColl	-.077	.159	.234	1	.629	.926	.678	1.265
Pct4yrColl	-.075	.159	.224	1	.636	.928	.679	1.266
MedIncome	.000	.000	.023	1	.878	1.000	1.000	1.000
MyoInfarc	-70.812	29296.083	.000	1	.998	.000	.000	.
OldMyoInfarc	-321.281	101671.885	.000	1	.997	.000	.000	.
CHF	-19.912	7638.910	.000	1	.998	.000	.000	.
COPD	.295	.478	.381	1	.537	1.343	.526	3.428
PeriphVascDisDx	1.978	1.589	1.550	1	.213	7.230	.321	162.832
CerebroVascDis	1.847	1.799	1.054	1	.305	6.338	.186	215.423
Dementia	-1.006	37528.289	.000	1	1.000	.366	.000	.
Paralysis	7.230	3.615	4.000	1	.046	1380.649	1.155	1649722.35
Diabetes	.213	1.574	.018	1	.892	1.237	.057	27.076
DiabetesSequelae	-3.102	2.841	1.192	1	.275	.045	.000	11.770
ChronicRenalFail	-25.503	21802.214	.000	1	.999	.000	.000	.
Rheum	6.498	6.768	.922	1	.337	663.980	.001	3.831E8
Constant	6.430	15.907	.163	1	.686	620.312		

a. Variable(s) entered on step 1: sPSA, Race, Grade, HistStageCombinary, MarStatus, Radiation, RadSurgCombinary, SurgCombinary, PctNonHSGrad, PctHSonly, PctSomeColl, Pct4yrColl, MedIncome, MyoInfarc, OldMyoInfarc, CHF, COPD, PeriphVascDisDx, CerebroVascDis, Dementia, Paralysis, Diabetes, DiabetesSequelae, ChronicRenalFail, Rheum.

Conditional Cox Regression for Age Quartile 3

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	124	4.0%
	Censored	64	2.1%
	Total	188	6.0%
Cases dropped	Cases with missing values	0	.0%

	Cases with negative time	0	.0%
	Censored cases before the earliest event in a stratum	2930	94.0%
	Total	2930	94.0%
Total		3118	100.0%

a. Dependent Variable: Survival time recode (total # of months)

Categorical Variable Codings[b,c,d,e]

		Frequency	(1)	(2)	(3)	(4)	(5)
Grade[a]	1	181	0				
	2	2937	1				
MarStatus[a]	1	164	0	0	0	0	0
	2	2186	1	0	0	0	0
	3	1	0	1	0	0	0
	4	84	0	0	1	0	0
	5	286	0	0	0	1	0
	9	397	0	0	0	0	1
Race[a]	1	2963	0				
	2	155	1				
Radiation[a]	0	1456	0	0	0	0	
	1	1133	1	0	0	0	
	2	279	0	1	0	0	
	4	224	0	0	1	0	
	9	26	0	0	0	1	

a. Indicator Parameter Coding
b. Category variable: Grade (Grade 1)
c. Category variable: MarStatus (Marital Status)
d. Category variable: Race (SEER Race Recode B)
e. Category variable: Radiation (Radiation 1)

Block 0: Beginning Block

Omnibus Tests of Model Coefficients
-2 Log Likelihood
94.268

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]

	Overall (score)			Change From Previous Step			Change From Previous Block		
-2 Log Likelihood	Chi-square	Df	Sig.	Chi-square	Df	Sig.	Chi-square	df	Sig.
54.384	29.175	27	.352	39.884	27	.053	39.884	27	.053

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
sPSA	-.719	.622	1.338	1	.247	.487	.144	1.648
Race	-5.510	5.535	.991	1	.320	.004	.000	208.210
Grade	4.821	2.123	5.157	1	.023	124.097	1.935	7959.05
HistStageCombine			.	0[a]	.			
MarStatus			4.586	4[a]	.332			
MarStatus(1)	-.289	3.295	.008	1	.930	.749	.001	477.498
MarStatus(3)	3.101	2.776	1.248	1	.264	22.212	.096	5120.85
MarStatus(4)	.783	2.924	.072	1	.789	2.189	.007	675.227
MarStatus(5)	-1.632	3.010	.294	1	.588	.196	.001	71.377
Radiation			1.003	3[a]	.800			
Radiation(1)	-.296	.823	.129	1	.719	.744	.148	3.729
Radiation(2)	.792	3.095	.065	1	.798	2.207	.005	950.664
Radiation(3)	-.919	1.325	.481	1	.488	.399	.030	5.352
RadSurgCombine	2.853	2.258	1.596	1	.206	17.345	.207	1450.46

SurgCombinary	-5.766	4.870	1.402	1	.236	.003	.000	43.747
Hormones			.	0[a]	.			
PctNonHSGrad	-1.523	.667	5.219	1	.022	.218	.059	.805
PctHSonly	-1.545	.694	4.956	1	.026	.213	.055	.831
PctSomeColl	-1.400	.638	4.818	1	.028	.247	.071	.861
Pct4yrColl	-1.354	.630	4.620	1	.032	.258	.075	.888
MedIncome	.000	.000	2.010	1	.156	1.000	1.000	1.000
MyoInfarc	-57.309	678.800	.007	1	.933	.000	.000	.
OldMyoInfarc	-243.409	3042.471	.006	1	.936	.000	.000	.
CHF	-18.248	188.057	.009	1	.923	.000	.000	1.412E152
PeriphVascDisDx	3.467	5.907	.345	1	.557	32.050	.000	3415693.
CerebroVascDis	24.444	340.227	.005	1	.943	4.129E1	.000	1.649E300
COPD	-4.417	3.924	1.267	1	.260	.012	.000	26.440
Dementia			.	0[a]	.			
Paralysis	-3.860	759.718	.000	1	.996	.021	.000	.
Diabetes	.514	6.567	.006	1	.938	1.673	.000	650271.66
DiabetesSequelae	-12.457	373.365	.001	1	.973	.000	.000	.
ChronicRenalFail			.	0[a]	.			
Rheum	-145.246	1805.370	.006	1	.936	.000	.000	.
a. Degree of freedom reduced because of constant or linearly dependent covariates								

Appendix K

Logistic and Conditional Cox Regression with Propensity Analysis

AGE Quartile 4

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	664	100.0
	Missing Cases	0	.0
	Total	664	100.0
Unselected Cases		0	.0
Total		664	100.0

a. If weight is in effect, see classification table for the total number of cases.

b. The variable HistStageCombinary is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

c. The variable Hormones is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

d. The variable DEMENTIA (1) is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

e. The variable PARALYSIS (1) is constant for the selected cases. Since a constant term was specified, the variable will be removed from the analysis.

Dependent Variable Encoding

Original Value	Internal Value
0	0
1	1

Categorical Variables Codings

			Parameter coding				
		Frequency	(1)	(2)	(3)	(4)	(5)
Marital Status	1	24	.000	.000	.000	.000	.000
	2	404	1.000	.000	.000	.000	.000
	3	1	.000	1.000	.000	.000	.000
	4	13	.000	.000	1.000	.000	.000
	5	107	.000	.000	.000	1.000	.000
	9	115	.000	.000	.000	.000	1.000
Radiation 1	0	489	.000	.000	.000	.000	
	1	116	1.000	.000	.000	.000	
	2	27	.000	1.000	.000	.000	
	4	20	.000	.000	1.000	.000	
	9	12	.000	.000	.000	1.000	
Grade 1	1	41	.000				
	2	623	1.000				
SEER Race Recode	1	631	.000				
	2	33	1.000				

Block 0: Beginning Block

Classification Table[a,b]

			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 0	Mortality	0	625	0	100.0
		1	39	0	.0
	Overall Percentage				94.1

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-2.774	.165	282.520	1	.000	.062

Variables not in the Equation[a]

		Score	df	Sig.
Step 0	sPSA	.027	1	.869
	Grade(1)	1.192	1	.275
	MarStatus	3.995	5	.550
	MarStatus(1)	1.223	1	.269
	MarStatus(2)	.062	1	.803
	MarStatus(3)	.079	1	.778
	MarStatus(4)	3.700	1	.054
	MarStatus(5)	.011	1	.915
	Race(1)	.508	1	.476
	Radiation	.881	1	.348
	RadSurgCombinary	.906	1	.341
	SurgCombinary	6.221	1	.013
	PctNonHSGrad	3.259	1	.071
	PctHSonly	1.820	1	.177
	PctSomeColl	.143	1	.705
	Pct4yrColl	2.886	1	.089
	MedIncome	1.399	1	.237
	MyoInfarc	.453	1	.501
	OldMyoInfarc	.134	1	.715
	CHF	.505	1	.477
	PeriphVascDisDx	.958	1	.328
	CerebroVascDis	.746	1	.388
	COPD	1.321	1	.250
	Diabetes	.131	1	.718
	DiabetesSequelae	.453	1	.501
	ChronicRenalFail	.062	1	.803
	Rheum	.188	1	.665

a. Residual Chi-Squares are not computed because of redundancies.

Block 1: Method = Enter

Omnibus Tests of Model Coefficients				
		Chi-square	Df	Sig.
Step 1	Step	26.484	29	.600
	Block	26.484	29	.600
	Model	26.484	29	.600

Model Summary			
Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	270.287[a]	.039	.108
a. Estimation terminated at iteration number 20 because maximum iterations have been reached. Final solution cannot be found.			

Classification Table[a]				
			Predicted	
			Mortality	Percentage
	Observed		0	1	Correct
Step 1	Mortality	0	625	0	100.0
		1	39	0	.0
	Overall Percentage				94.1
a. The cut value is .500					

Variables in the Equation								
							95% C.I. for Exp(B)	
	B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
sPSA	-.060	.353	.029	1	.865	.942	.472	1.88
Race(1)	-.277	1.077	.066	1	.797	.758	.092	6.25
Grade(1)	-.347	.607	.326	1	.568	.707	.215	2.32
MarStatus			3.345	5	.647			
MarStatus(1)	-.356	.803	.197	1	.657	.700	.145	3.38
MarStatus(2)	-18.534	40192.970	.000	1	1.000	.000	.000	.

MarStatus(3)	-.223	1.363	.027	1	.870	.800	.055	11.5
MarStatus(4)	-1.651	1.065	2.403	1	.121	.192	.024	1.54
MarStatus(5)	-.301	.876	.118	1	.731	.740	.133	4.11
Radiation			2.938	4	.568			
Radiation(1)	-1.015	.654	2.410	1	.121	.362	.101	1.30
Radiation(2)	-.613	1.077	.323	1	.570	.542	.066	4.47
Radiation(3)	.277	.886	.097	1	.755	1.319	.232	7.48
Radiation(4)	-18.840	11416.158	.000	1	.999	.000	.000	.
RadSurgCombine	1.201	1.456	.680	1	.409	3.324	.191	57.7
SurgCombinary	.813	.414	3.844	1	.050	2.254	1.000	5.07
PctNonHSGrad	-.059	.291	.042	1	.839	.942	.533	1.66
PctHSonly	-.030	.295	.010	1	.919	.970	.544	1.73
PctSomeColl	-.025	.293	.008	1	.931	.975	.549	1.73
Pct4yrColl	-.028	.294	.009	1	.924	.972	.546	1.73
MedIncome	.000	.000	.030	1	.862	1.000	1.000	1.00
MyoInfarc	.786	5.308	.022	1	.882	2.196	.000	7240
OldMyoInfarc	8.969	23.431	.147	1	.702	7856.324	.000	6.91E23
CHF	-21.449	15560.851	.000	1	.999	.000	.000	.
PeriphVascDisDx	-52.916	26669.750	.000	1	.998	.000	.000	.
CerebroVascDis	1.767	2.712	.425	1	.515	5.855	.029	1192
COPD	.567	.793	.511	1	.475	1.764	.372	8.35
Diabetes	-.048	3.149	.000	1	.988	.953	.002	456.
DiabetesSequelae	3.356	3.023	1.232	1	.267	28.663	.077	10729
ChronicRenalFail	-27.313	59281.667	.000	1	1.000	.000	.000	.
Rheum	-202.616	249679.247	.000	1	.999	.000	.000	.
Constant	1.313	29.214	.002	1	.964	3.717		

a. Variable(s) entered on step 1: sPSA, Race, Grade, MarStatus, Radiation, RadSurgCombinary, SurgCombinary, PctNonHSGrad, PctHSonly, PctSomeColl, Pct4yrColl, MedIncome, MyoInfarc, OldMyoInfarc, CHF, PeriphVascDisDx, CerebroVascDis, COPD, Diabetes, DiabetesSequelae, ChronicRenalFail, Rheum.

Conditional Cox Regression for Age Quartile 4

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	39	5.9%
	Censored	22	3.3%
	Total	61	9.2%
Cases dropped	Cases with missing values	0	.0%
	Cases with negative time	0	.0%
	Censored cases before the earliest event in a stratum	603	90.8%
	Total	603	90.8%
Total		664	100.0%

a. Dependent Variable: Survival time recode (total # of months)

Categorical Variable Codings[b,c,d,e]

		Frequency	(1)	(2)	(3)	(4)	(5)
Grade[a]	1	41	0				
	2	623	1				
MarStatus[a]	1	24	0	0	0	0	0
	2	404	1	0	0	0	0
	3	1	0	1	0	0	0
	4	13	0	0	1	0	0
	5	107	0	0	0	1	0
	9	115	0	0	0	0	1
Race[a]	1	631	0				
	2	33	1				
Radiation[a]	0	489	0	0	0	0	
	1	116	1	0	0	0	
	2	27	0	1	0	0	
	4	20	0	0	1	0	
	9	12	0	0	0	1	

a. Indicator Parameter Coding

b. Category variable: Grade (Grade 1)
c. Category variable: MarStatus (Marital Status)
d. Category variable: Race (SEER Race Recode B)
e. Category variable: Radiation (Radiation 1)

Block 0: Beginning Block

Omnibus Tests of Model Coefficients
-2 Log Likelihood
33.271

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]

	Overall (score)			Change From Previous Step			Change From Previous Block		
-2 Log Likelihood	Chi-square	df	Sig.	Chi-square	Df	Sig.	Chi-square	df	Sig.
33.271	19.424	21	.558	.000	21	1.000	.000	21	1.000

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
sPSA	.000	1.200	.000	1	1.000	1.000	.095	10.511
Race	.000	12.92	.000	1	1.000	1.000	.000	9.951E10
Grade	.000	4.051	.000	1	1.000	1.000	.000	2805.46
HistStageCombined			.	0[a]	.			
MarStatus			.000	4[a]	1.000			
MarStatus(1)	.000	6.804	.000	1	1.000	1.000	.000	618847.5
MarStatus(3)	.000	6.795	.000	1	1.000	1.000	.000	608551.
MarStatus(4)	.000	7.729	.000	1	1.000	1.000	.000	3795993

MarStatus(5)	.000	8.064	.000	1	1.000	1.000	.000	7318555
Radiation			.000	3[a]	1.000			
Radiation(1)	.000	2.135	.000	1	1.000	1.000	.015	65.607
Radiation(2)	.000	6.085	.000	1	1.000	1.000	.000	151081
Radiation(3)	.000	3.353	.000	1	1.000	1.000	.001	715.290
RadSurgCombinary	.000	5.186	.000	1	1.000	1.000	.000	25971
SurgCombinary	.000	10.31	.000	1	1.000	1.000	.000	5.984E8
Hormones			.	0[a]	.			
PctNonHSGrad	.000	2.245	.000	1	1.000	1.000	.012	81.466
PctHSonly	.000	2.081	.000	1	1.000	1.000	.017	59.048
PctSomeColl	.000	2.230	.000	1	1.000	1.000	.013	79.137
Pct4yrColl	.000	2.182	.000	1	1.000	1.000	.014	72.032
MedIncome	.000	.000	.000	1	1.000	1.000	1.000	1.000
MyoInfarc			.	0[a]	.			
OldMyoInfarc			.	0[a]	.			
CHF	.000	19.91	.000	1	1.000	1.000	.000	9.016E16
PeriphVascDisDx	.000	15.00	.000	1	1.000	1.000	.000	5.940E12
CerebroVascDis	.000	37.30	.000	1	1.000	1.000	.000	5.654E31
COPD	.000	8.316	.000	1	1.000	1.000	.000	1.198E7
Dementia			.	0[a]	.			
Paralysis			.	0[a]	.			
DiabetesSequelae			.	0[a]	.			
ChronicRenalFail			.	0[a]	.			
Rheum			.	0[a]	.			

a. Degree of freedom reduced because of constant or linearly dependent covariates

Appendix L

Logistic Regression: Non Cancer Group–No Propensity Analysis

Case Processing Summary			
Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	15557	100.0
	Missing Cases	0	.0
	Total	15557	100.0
Unselected Cases		0	.0
Total		15557	100.0
a. If weight is in effect, see classification table for the total number of cases.			

Dependent Variable Encoding	
Original Value	Internal Value
0	0
1	1

Categorical Variables Codings						
			Parameter coding			
		Frequency	(1)	(2)	(3)	(4)
age category	14	750	.000	.000	.000	.000
	15	2074	1.000	.000	.000	.000
	16	2873	.000	1.000	.000	.000
	17	5920	.000	.000	1.000	.000
	18	3940	.000	.000	.000	1.000
Race	1	14276	.000			
	2	1281	1.000			

Block 0: Beginning Block

Classification Table[a,b]				
		Predicted		
		Mortality		Percentage
Observed		0	1	Correct
Mortality	0	8803	0	100.0
	1	6754	0	.0
Overall Percentage				56.6
a. Constant is included in the model.				
b. The cut value is .500				

Variables in the Equation							
		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-.265	.016	268.299	1	.000	.767

Variables not in the Equation[a]					
			Score	df	Sig.
Step 0	Variables	sPSA	113.425	1	.000
		Race(1)	16.420	1	.000
		Age(66-69yrs)	2320.165	4	.000
		Age(70-74yrs)	551.340	1	.000
		Age(75-79yrs)	220.610	1	.000
		Age(80-84yrs)	.759	1	.384
		Age(85+)	1761.868	1	.000
		NoHighSchool	18.742	1	.000
		HighSchool	6.411	1	.011
		SomeCollege	5.792	1	.016
		College4yrs	15.151	1	.000
		MedInc	6.987	1	.008
		Myocardial	1.287	1	.257
		OldMyocardial	.129	1	.720
		CHF	114.608	1	.000
		CerbroVascDs	43.775	1	.000
		COPD	91.624	1	.000

		Dementia	52.186	1	.000
		Paralysis	15.022	1	.000
		Diabetes	10.873	1	.001
		DiabetesSequelae	46.897	1	.000
		ChronicRenalFail	26.550	1	.000
		Rheumatology	.709	1	.400
a. Residual Chi-Squares are not computed because of redundancies.					

Block 1: Method = Enter

Omnibus Tests of Model Coefficients				
		Chi-square	df	Sig.
Step 1	Step	2943.796	22	.000
	Block	2943.796	22	.000
	Model	2943.796	22	.000

Model Summary			
Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	18352.127[a]	.172	.231
a. Estimation terminated at iteration number 5 because parameter estimates changed by less than .001.			

Classification Table[a]					
			Predicted		
			mortality		Percentage
	Observed		0	1	Correct
Step 1	mortality	0	7071	1732	80.3
		1	3184	3570	52.9
	Overall Percentage				68.4
a. The cut value is .500					

Variables in the Equation								
							95% C.I. for Exp(B)	
	B	S.E.	Wald	Df	Sig.	Exp(B)	Lower	Upper
sPSA	-.257	.040	40.611	1	.000	.774	.715	.837
Race(1)	.354	.066	28.436	1	.000	1.424	1.251	1.622
AGE(66-69yrs)			2033.366	4	.000			
AGE(70-74yrs)	.868	.137	40.121	1	.000	2.381	1.820	3.114
AGE(75-79yrs)	1.542	.132	137.017	1	.000	4.674	3.610	6.050
AGE(80-84yrs)	2.091	.128	266.050	1	.000	8.096	6.297	10.409
AGE(85+)	3.331	.131	648.136	1	.000	27.958	21.635	36.130
NoHighSchool	.014	.015	.947	1	.330	1.015	.985	1.044
HighSchool	.014	.015	.823	1	.364	1.014	.984	1.044
SomeCollege	.007	.015	.218	1	.641	1.007	.978	1.037
College4yrs	.003	.015	.030	1	.863	1.003	.974	1.032
MedInc	.000	.000	7.693	1	.006	1.000	1.000	1.000
Myocardial	-.512	.310	2.733	1	.098	.599	.327	1.100
OldMyocardial	.110	1.162	.009	1	.924	1.117	.115	10.886
CHF	.459	.064	51.969	1	.000	1.583	1.397	1.794
PeriphlVascDs	.512	.210	5.948	1	.015	1.669	1.106	2.520
CerbroVascDs	.813	.201	16.335	1	.000	2.254	1.520	3.342
COPD	.563	.063	79.963	1	.000	1.757	1.553	1.988
Dementia	.895	.182	24.112	1	.000	2.448	1.712	3.499
Diabetes	1.320	.199	43.838	1	.000	3.743	2.533	5.533
DiabetesSeque	1.454	.216	45.530	1	.000	4.282	2.807	6.533
ChronRenFail	.571	.200	8.195	1	.004	1.771	1.197	2.618
Rheumatology	2.490	1.739	2.052	1	.152	12.067	.400	364.38
Constant	-3.579	1.478	5.866	1	.015	.028		

a. Variable(s) entered on step 1: sPSA, Race, AGE (66-69yrs), NoHighSchool, HighSchool, SomeCollege, College4yrs, MedInc, Myocardial, OldMyocardial, CHF, PeripheralVascDs, CerbroVascDs, COPD, Dementia, Diabetes, DiabetesSequelae, ChronicRenalFailure, Rheumatology.

Cox Regression: Non-Cancer-Non Propensity Analysis

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	6754	43.4%
	Censored	8803	56.6%
	Total	15557	100.0%
Cases dropped	Cases with missing values	0	.0%
	Cases with negative time	0	.0%
	Censored cases before the earliest event in a stratum	0	.0%
	Total	0	.0%
Total		15557	100.0%

a. Dependent Variable: survival months

Categorical Variable Codings[b,c]

		Frequency	(1)	(2)	(3)	(4)
Race[a]	1	14276	0			
	2	1281	1			
Age[a]	14	750	0	0	0	0
	15	2074	1	0	0	0
	16	2873	0	1	0	0
	17	5920	0	0	1	0
	18	3940	0	0	0	1

a. Indicator Parameter Coding

b. Category variable: Race (race)

c. Category variable: AGE Cat (age category)

Block 0: Beginning Block

Omnibus Tests of Model Coefficients
-2 Log Likelihood
111926.818

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]									
	Overall (score)			Change From Previous Step			Change From Previous Block		
-2 Log Likelihood	Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
104553.341	9511.482	23	.000	7373.478	23	.000	7373.478	23	.000
a. Beginning Block Number 1. Method = Enter									

Variables in the Equation								
							95.0% CI for Exp(B)	
	B	SE	Wald	Df	Sig.	Exp(B)	Lower	Upper
sPSA	.085	.028	9.395	1	.002	1.089	1.031	1.149
Race	.090	.045	3.964	1	.046	1.094	1.001	1.195
Age(66-69yrs)			7410.66	4	.000			
Age(70-74yrs)	1.665	.146	130.042	1	.000	5.286	3.970	7.037
Age(75-79yrs)	1.376	.152	81.974	1	.000	3.960	2.939	5.334
Age(80-84yrs)	-.937	.145	41.859	1	.000	.392	.295	.521
Age(85+)	-3.407	.136	628.743	1	.000	.033	.025	.043
NoHighSchool	-.045	.009	23.395	1	.000	.956	.939	.974
HighSchool	-.044	.009	21.356	1	.000	.957	.940	.975
SomeCollege	-.054	.009	32.186	1	.000	.948	.930	.966
College4yrs	-.041	.009	19.459	1	.000	.959	.942	.977
MedInc	.000	.000	30.651	1	.000	1.000	1.000	1.000

Myocardial	.299	.216	1.931	1	.165	1.349	.884	2.058
OldMyocardial	1.823	.797	5.226	1	.022	6.189	1.297	29.535
CHF	.134	.040	11.031	1	.001	1.143	1.056	1.237
PeriphVascDs	.099	.135	.541	1	.462	1.104	.848	1.438
CerbroVascDs	.396	.143	7.631	1	.006	1.486	1.122	1.969
COPD	.347	.041	71.518	1	.000	1.415	1.306	1.534
Dementia	.108	.100	1.158	1	.282	1.114	.915	1.354
Paralysis	.141	.186	.575	1	.448	1.151	.800	1.657
Diabetes	1.208	.135	80.218	1	.000	3.346	2.569	4.357
Diabetes Sequela	.896	.131	46.620	1	.000	2.450	1.894	3.168
ChronicRenfail	.339	.119	8.187	1	.004	1.404	1.113	1.771
Rheumatology	3.684	1.172	9.878	1	.002	39.804	4.001	395.963

Appendix M

Logistic and Conditional Cox Regression: Non Cancer Group with Propensity Analysis

Logistic Regression Output

Case Processing Summary			
Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	8426	100.0
	Missing Cases	0	.0
	Total	8426	100.0
Unselected Cases		0	.0
Total		8426	100.0
a. If weight is in effect, see classification table for the total number of cases.			

Dependent Variable Encoding	
Original Value	Internal Value
0	0
1	1

Categorical Variables Codings						
			Parameter coding			
		Frequency	(1)	(2)	(3)	(4)
age	66-69yrs	355	.000	.000	.000	.000
category	70-74yrs	945	1.000	.000	.000	.000
	75-79yrs	1393	.000	1.000	.000	.000
	80-84yrs	3079	.000	.000	1.000	.000
	85+	2654	.000	.000	.000	1.000
Race	1 Cauc.	7514	.000			
	2 AA	912	1.000			

Block 0: Beginning Block

Classification Table[a,b]					
			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 0	mortality	0	4416	0	100.0
		1	4010	0	.0
	Overall Percentage				52.4
a. Constant is included in the model.					
b. The cut value is .500					

Variables in the Equation							
		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-.096	.022	19.548	1	.000	.908

Variables not in the Equation[a]					
			Score	Df	Sig.
Step 0	Variables	sPSA	25.380	1	.000
		Race(1)	8.276	1	.004
		AGE (66-69yrs)	1296.899	4	.000
		AGE (70-74yrs)	293.270	1	.000
		AGE (75-79yrs)	160.792	1	.000
		AGE (80-84yrs)	18.255	1	.000
		AGE (85+)	1034.592	1	.000
		NoHighSchool	13.662	1	.000
		HighSchool	7.533	1	.006
		SomeCollege	9.588	1	.002
		College4yrs	10.969	1	.001
		MedInc	6.629	1	.010
		Myocardial	3.483	1	.062
		OldMyocardial	.444	1	.505
		CHF	90.151	1	.000
		PeripheralVascDs	11.004	1	.001

	CerbroVascDs	22.323	1	.000
	COPD	57.370	1	.000
	Dementia	29.845	1	.000
	Paralysis	12.239	1	.000
	Diabetes	6.454	1	.011
	DiabetesSequelae	23.218	1	.000
	ChronicRenalFail	11.906	1	.001
	Rheumatology	.245	1	.621
a. Residual Chi-Squares are not computed because of redundancies.				

Block 1: Method = Enter

Omnibus Tests of Model Coefficients				
		Chi-square	Df	Sig.
Step 1	Step	1698.668	23	.000
	Block	1698.668	23	.000
	Model	1698.668	23	.000

Model Summary			
Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	9962.678[a]	.183	.244
a. Estimation terminated at iteration number 5 because parameter estimates changed by less than .001.			

Classification Table[a]					
			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 1	mortality	0	3295	1121	74.6
		1	1555	2455	61.2
	Overall Percentage				68.2

Classification Table[a]					
			Predicted		
			Mortality		Percentage
	Observed		0	1	Correct
Step 1	mortality	0	3295	1121	74.6
		1	1555	2455	61.2
	Overall Percentage				68.2
a. The cut value is .500					

Variables in the Equation									
								95% C.I. for Exp(B)	
		B	S.E.	Wald	Df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	sPSA	-.281	.049	33.464	1	.000	.755	.686	.830
	Race(1)	.371	.080	21.524	1	.000	1.449	1.239	1.695
	Age(66-69yrs)			1183.5	4	.000			
	Age (70-74yrs)	.755	.186	16.464	1	.000	2.127	1.477	3.062
	Age (75-79yrs)	1.403	.178	62.311	1	.000	4.067	2.871	5.761
	Age (80-84yrs)	1.968	.172	130.61	1	.000	7.159	5.108	10.034
	Age (85+)	3.248	.175	345.71	1	.000	25.733	18.273	36.239
	NoHighSchool	.006	.015	.173	1	.677	1.006	.977	1.037
	HighSchool	.010	.015	.451	1	.502	1.010	.980	1.041
	SomeCollege	-.002	.015	.012	1	.912	.998	.969	1.029
	College4yrs	-.002	.015	.014	1	.904	.998	.969	1.028
	MedInc	.000	.000	1.504	1	.220	1.000	1.000	1.000
	Myocardial	-1.074	.439	5.984	1	.014	.342	.145	.808
	OldMyocardial	-.642	1.596	.162	1	.688	.526	.023	12.026
	CHF	.597	.086	48.457	1	.000	1.816	1.535	2.149
	PeriphlVascDs	.369	.300	1.512	1	.219	1.446	.803	2.603
	CerbroVascDs	.762	.298	6.532	1	.011	2.143	1.194	3.844
	COPD	.586	.085	47.739	1	.000	1.796	1.521	2.121
	Dementia	.830	.231	12.894	1	.000	2.293	1.458	3.606
	Paralysis	.253	.379	.446	1	.504	1.288	.613	2.709
	Diabetes	1.527	.272	31.506	1	.000	4.605	2.702	7.848
	DiabetesSequel	1.338	.286	21.892	1	.000	3.810	2.175	6.671

	ChronicRenFail	.453	.241	3.532	1	.060	1.573	.981	2.524
	Rheumatology	3.214	2.372	1.836	1	.175	24.877	.238	2600.4
	Constant	-2.805	1.512	3.442	1	.064	.061		
a. Variable(s) entered on step 1: sPSA, Race, Age (66-69yrs), NoHighSchool, HighSchool, SomeCollege, College4yrs, MedInc, Myocardial, OldMyocardial, CHF, PeripheralVascDs, CerbroVascDs, COPD, Dementia, Paralysis, Diabetes, DiabetesSequelae, ChronicRenalFailure, Rheumatology.									

Conditional Cox Regression Output

Case Processing Summary			
		N	Percent
Cases available in analysis	Event[a]	4010	47.6%
	Censored	688	8.2%
	Total	4698	55.8%
Cases dropped	Cases with missing values	0	.0%
	Cases with negative time	0	.0%
	Censored cases before the earliest event in a stratum	3728	44.2%
	Total	3728	44.2%
Total		8426	100.0%
a. Dependent Variable: survtimemonths			

Categorical Variable Codings[b,c]						
		Frequency	(1)	(2)	(3)	(4)
Race[a]	1Cauc	7514	0			
	2 AA	912	1			
Age Cat	66-69	355	0	0	0	0
	70-74	945	1	0	0	0
	75-79	1393	0	1	0	0
	80-84	3079	0	0	1	0

	85+	2654	0	0	0	1
a. Indicator Parameter Coding						
b. Category variable: Race (Race)						
c. Category variable: AGE Cat (age category)						

Block 0: Beginning Block

Omnibus Tests of Model Coefficients
-2 Log Likelihood
2524.442

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]									
	Overall (score)			Change From Previous Step			Change From Previous Block		
-2 Log Likelihood	Chi-square	Df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
1403.481	708.829	23	.000	1120.96	23	.000	1120.961	23	.000
a. Beginning Block Number 1. Method = Enter									

Variables in the Equation								
							95.0% CI for Exp(B)	
	B	SE	Wald	Df	Sig.	Exp(B)	Lower	Upper
sPSA	-.048	.064	.578	1	.447	.953	.841	1.079
Race	1.068	5.038	.045	1	.832	2.911	.000	56566.767
Age(66-69yrs)			11.617	4	.020			
Age(70-74yrs)	-5.826	4.927	1.398	1	.237	.003	.000	46.075
Age(75-79yrs)	-11.47	6.095	3.541	1	.060	.000	.000	1.610
Age(80-84yrs)	-17.43	7.199	5.867	1	.015	.000	.000	.036
Age(85+)	-24.02	8.392	8.193	1	.004	.000	.000	.001

NoHighSchool	.045	.031	2.036	1	.154	1.046	.983	1.112
HighSchool	.050	.041	1.465	1	.226	1.051	.970	1.139
SomeCollege	.036	.081	.203	1	.652	1.037	.885	1.215
College4yrs	.041	.035	1.357	1	.244	1.041	.973	1.115
MedInc	.000	.000	.702	1	.402	1.000	1.000	1.000
Myocardial	.471	8.082	.003	1	.954	1.601	.000	1.213E7
OldMyocardial	2.386	15.80	.023	1	.880	10.865	.000	3.058E14
CHF	.224	1.094	.042	1	.838	1.251	.147	10.675
PeriphVascDs	-1.104	5.475	.041	1	.840	.332	.000	15167.984
CerbroVascDs	-.097	3.886	.001	1	.980	.908	.000	1843.893
COPD	.302	1.149	.069	1	.793	1.352	.142	12.856
Dementia	-.001	2.059	.000	1	1.000	.999	.018	56.565
Paralysis	1.631	6.986	.055	1	.815	5.110	.000	4519734.8
Diabetes	2.173	1.032	4.434	1	.035	8.788	1.162	66.437
DiabetesSequelae	1.057	3.587	.087	1	.768	2.879	.003	3256.562
ChronicRenalFail	1.212	5.944	.042	1	.838	3.360	.000	385305.99
Rheumatology	18.659	27.98	.445	1	.505	1.269E8	.000	8.349E31

VITA

R. David McNally was born on December 18, 1961 in Rantoul, Illinois. He graduated with a Bachelor of Science in Nuclear Medicine from the Medical College of Georgia in Augusta Georgia in 1985. In 1987, he earned a Master of Science in Medical Physics from the Georgia Institute of Technology in Atlanta Georgia after completing relevant coursework and a thesis on control of bio-fouling bacteria in industrial well systems using radioactive source materials. He went on to earn a second Master of Science in Health Services Administration from Armstrong Atlantic State University in Savannah Georgia in 2002. During the completion of his doctoral studies, he has served as a medical physicist and manager of a cancer center.